Risks, Benefits and Current Management Strategies of Statin Therapy

Katherine Gambino, CRNP
Erin Henry, CRNP
Teri Miller, CRNP
Objectives

- Participant will be able to verbalize the latest guidelines for statin therapy
- Participant will be able to state the benefits of statins in terms of reducing cardiovascular morbidity and mortality
- Participant will be able to state the adverse effects/intolerances related to statin use
- Participant will be able to describe the current practice patterns regarding the use of statin therapy in the Cleveland Clinic Preventive Cardiology.
The statins!!!!!!!
What are statins?

• Statins inhibit the HMG-CoA reductase enzyme therefore reducing the production of cholesterol in the liver.
• Metabolized in the liver
• Impact all components of a lipid panel (TC, TG, HDL, LDL) but mostly the LDL.
• Reduces LDL by 25-63%
FDA Indications

• Labeled indications:
  - Prevention of cardiovascular disease
  - Treatment of dyslipidemia
  - Treatment of heterozygous familial hypercholesterolemia.

• Primary prevention: Lipid reduction before disease occurs

• Secondary prevention: After the development of disease
Just 3 simple rules, folks:
1. It must work.
2. It must be safe.
3. It must not be “fun.”

Of course, there’s wiggle room on 1 & 2.

DRUG APPROVAL

F.D.A. TRAINING
What are the statins?

• Rosuvastatin (Crestor) – high potency
• Atorvastatin (Lipitor) – high potency
• Simvastatin (Zocor)
• Pravastatin (Pravachol)
• Lovastatin (Mevacor)
• Pitavastatin (Livalo)
• Fluvastatin (Lescol XL)
Trivia question!!

• Trivia question

• What was the first statin, and when was it FDA approved for use?
Primary Prevention Trials

- **EPIDEMIOLOGIC STUDIES**

- **WOSCOPS** Pravastatin 40mg reduced non-fatal MI/CHD mortality in men with LDLs >155.

- **AFCAPS/TEXCAPS** Lovastatin 20-40mg reduced incidence 1st major CVE in low risk male/females, average LDL 150s with lower HDLs.

- **ASCOT LAA** Atorvastatin 10mg reduced MI/total CVE/Stoke in htn patients or those with 3+ risk factors.

- **JUPITOR** 15,000 patients multicenter trial, rosuvastatin 20mg in those with LDL<130 and CRP >2.0 showed marked reduction 1st CVE: MI, CVA, need for CABG PTCA, all cause mortality. Those taking statin compared with placebo had 54% lower chance MI, 48% CVA, 46% PTCA/CABG/20% dying any cause. Stopped early. Normal LDL, inc CRP benefit.

- **METEOR** Rosuvastatin in low risk groups comparing CIMT; stat sign diff CIMT and LDL.
Secondary Prevention Trials

- **4S** Simvastatin 20-40mg reduced total mortality, coronary events, CHD deaths, need for revasc in 4444 subjects with recent MI/angina.

- **CARE** Pravastatin 40mg reduced coronary death, non fatal MI, need revasc, CVA/TIA in 4159 subjects with hx MI.

- **LIPID** Pravastatin reduced death from CHD, total mortality, CVA, bypass, fatal/non fatal MI in >9000 subjects with recent MI/UA. Stopped early.

- **HPS** Simvastatin 40mg reduced all cause mortality, death from ht or blood vessel disease, major CVE, CVA in 20,536 subjects with hx CVD (cor/perip/cere), DM or Htn (mostly secondary prevention). **Red in events similar in all tertiles LDL** (including all cause mortality, as well as low CRP and LDL).

- **Post CABG Trial extended follow up period** 1351 patients, lovastatin reduced composite endpt: death/MI/revasc stroke 18% end trial; 24% at 7.5 years (significant p = .0001).
Regression Trials Statins

- **REGRESS**  Pravastatin 40mg delayed progression CAD, showed lower rate progression periph/carotid disease, less CVEs, with 42% red non-fatal MI(not stat sig), red progression PVD.

- **LCAS**  Fluvastatin reduced progression on angio; low HDL benefit most.  429 patients over 2.5yrs

- **SCAT**  460 patients double randomiz simvastatin vs plac; and/or enal vs plac; simv less prgo/less PTCA. Normal cholesterol levels.

- **GAIN**  Intra u/s atorva red prog, inc hyperechogenicity of plaque (stable, less rupture) 131 pts 12

- **REVERSAL**  Atorva 80mg vs pravasatin 40mg. Mean change atheroma vol by IVUS sign lower atorvastatin group. (-0.4 vs 2.7); mean LDL significantly lower; 18 mos in 654 patients.

- **ASTEROID**  Open label controlled study. Rosuv 40mg red LDL 53%, median % atheroma vol decreased 0.79, most diseased segment -9.1%.  507 patients.
<table>
<thead>
<tr>
<th>hs-CRP Value</th>
<th>Cardiovascular Disease Risk Level*</th>
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<tbody>
<tr>
<td>&lt; 1 mg/L</td>
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<tr>
<td>1-3 mg/L</td>
<td>average risk</td>
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<tr>
<td>&gt; 3 mg/L</td>
<td>high risk</td>
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</table>

* Risk levels published in 2003. American Heart Association / Centers for Disease Control and Prevention Scientific Statement
Statins and usCRP

- **JUPITOR** Rosuvastatin 20mg LDL<130 and CRP ≥2.0 marked reduction 1st CVE: MI, CVA, need for CABG PTCA, all cause mortality. Those taking statin compared with placebo had 54% lower chance MI, 48% CVA, 46% PTCA/CABG/20% dying any cause. Stopped early. Normal LDL, inc CRP benefit.

- **AFCAPS** Lovastatin reduced CRP 15%.

- **PROVE IT-TIMI 22** Atorva 80mg vs prava 40mg in 4162 ACS patients.
  Both treatment groups significant reductions CRP. Linear relationship between levels CRP achieved after statin therapy and risk reduction of MI/death.
  After adjusting for LDL and CRP, CRP explained residual benefit associated with atorva –death/MI from CHD after 30 days.

- **REVERSAL** Atorva 80mg vs pravastatin 40mg. Much greater % change CRP with atorva. Any level LDL rate of progress lower in atorva group; suggesting factors other than LDL play role such as CRP.

- **A to Z trial** 4497 patients ACS. Simvastatin 40mg 80mg vs conservative strategy.
  - CRP at 30d and 4 months independently associated with long term survival
  - CRP >3.0 sig higher mort; higher statin with aggressive therapy more likely red CRP <1.3.
Lower LDLs the Better Trial
Secondary Prevention

• **TNT** 10,000 patients atorva 10mg vs 80mg.
  
  LDLs < 100 vs 75; significant reduction in primary endpoint MCVEs with aggressive targets for LDL.

• **PROVE-IT TIMI 22** prava 40mg vs atorava 80g in 4182 patients ACS
  
  LDLs <100 to LDLs <70. Significant reduction primary endpt with HR 0.84 in aggressive therapy group. 
  Primary endpoint death/MI/UA/revasc/CVA.

• **REVERSAL** Atorva 80mg vs pravastatin 40mg
  
  Progression atheroma IVUS correlated with reduction LDL; each 10% red LDL correlated with 1% red in change of atheoma volume. Supports lower LDLs.
Statins and Diabetes

- **Cholesterol Treatment Trialists Collaborators**
  Meta-analysis 18,686 DM patients revealed significant reductions of the following with statins:
  - major vasc events 21%, CVA 21%, major coronary event 22%, coronary revasc 25%

- **HPS** 3982 subjects. Simvastatin in subgroup with DM with no CVD reduced MI/CVA 28%.

- **CARDS** Atorva 10mg reduced CVEs in DM with no CVD 37%.
  - 2838 patients with additional risk (prot, sm, ret, htn), stopped early. LDL < > 120.

- **MEGA** 8214 Japanese men/post men females study diet vs pravastatin 10-20 in primary or DM reduced 1st occurrence CHD HR 0.67 Asian benefits similar to american.
Framingham Risk

CHD Risk: HDL-C Versus LDL-C as Predictor

*Data represent men aged 50–70 years from the Framingham Heart Study. CHD = coronary heart disease; RR = risk reduction.

Adapted from Castelli WP. Can J Cardiol. 1988(4 suppl A):SA-10A.
Trials Adding Therapy to Statins

**ACCORD**
- fenofib + statin vs statin
- 5 yrs.; no diff primary endpoint

**AIM HIGH**
- niacin + simva vs simva
- stopped early; no diff primary endpoint

**HPS Thrive**
- niacin + simva vs simva
- 4 yrs.; no diff primary endpoint

**ARBITOR 2**
- niacin + statin
- HDL increased 21%; CIMT –not stat sig

**CTEP INHIB TRIALS:**

**Dal Outcomes**
- dalcetrapib + statin vs statin
- 40% inc HDL; increased prim outcome stopped early futility

**Illuminate**
- torcetrapib + atorva vs atorva
- 72% inc in HDL; stopped early adv events

**ARBITOR 6-HALTS**
- niacin + statin vs ezetimibe + statin
- CHD or CHD risk equivalent with LDL<100; HDL < 50. Niacin red CIMT with fewer comp CV endpts (MI/revasc/ACS/death) p = 0.04.
Early Use of Statins After ACS
Large Randomized Trials

• **MIRACL**
  3086 patients with UA or non-Q wave MI
  Atorva 80mg vs placebo.
  Atorva 80mg reduced symptomatic ischemia requiring hospitalization;
  not death, resuscitation after arrest or MI/ revascularization

• **PROVE IT-TIMI 22:**
  compared atorvastatin 80mg with pravasatin 40mg in 4162 patients with ACS
  LDL lower:  62 vs 96
  combined endpoint (death any cause, MI, UA coronary revasc,CVA ) sign lower atorvastatin group
  with HR 0.84   CRP lower with atrovastatin.
Reduction in Stroke

• SPARCL: Atorvastatin reduced stroke, CAD events. No reduction in all cause mortality.
• HPS: Simvastatin reduced risk of first stroke (ischemic) compared to placebo.
• CARE: Pravastatin reduced risk of CAD event, CVA and CVA + TIA.
• ASCOTT-LLA: In high risk primary prev. patients with HTN and normal lipids, the risk of CVA was lower with Atorvastatin than placebo.
Pleiotropic benefits

• Plaque stabilization
• Reduces inflammation
• Improves endothelial function
• Promotes angiogenesis
• Repair endothelial injury
• Stabilizes arterial plaque
• Prevents cardiovascular and cerebrovascular events
Side Effects

Maybe you’ll start feeling better if you stop reading WebMD.

someecards
Don't let Big Pharma ruin your health. Wake up to the cholesterol con!

STATINS KILL !!!

CHOLESTEROL DOES NOT know

Educate yourself: things.org, stopped_our_statins, statins side effects

Beware the Statin Pushers

$STATIN NATION
The Great Cholesterol Cover-Up

The Dark Side of Statins
by Deane Graveline MD, MPH

The Great Cholesterol Con
THE TRUTH ABOUT WHAT REALLY CAUSES HEART DISEASE AND HOW TO AVOID IT
DR MALCOLM KENDRICK
Hepatic Dysfunction

• High aminotransferases (ALT)
• 0.5-3% occurrence of persistent elevations of LFT’s in patients on statins.
  – Highest occurrence first 3-4 months of therapy
• Overall incidence of hepatic failure is no different than the incidence in the general population.
• FDA recommended in 2012 to check LFT’s prior to initiating statin therapy and when clinically indicated (fatty liver disease, statin intolerance, prior history of elevations).
• Routine LFT monitoring is not indicated.
• Change or lower statin dose if ALT > 3x ULN
Myopathic Syndromes

- **Myalgia**: Muscle discomfort (aches, soreness, stiffness, tenderness) with a normal CK
  - 2-11% chance. Resolves days to weeks after discontinuing

- **Myopathy**: Muscle weakness with or without CK elevation

- **Myositis**: Muscle inflammation (with elevated CK)
  - 0.5% chance

- **Myonecrosis**: Elevated CK compared with baseline
  - Clinically significant if CK is > 10 times normal with muscle symptoms
  - Occurs in < 0.5% of patients in clinical trials
Rhabdomyolysis

• Rhabdomyolysis: Myonecrosis with myoglobinuria or ARF.
  – < 0.1% chance

• Rhabdomyolysis with ARF has primarily been seen when a statin is used with cyclosporine, gemfibrozil or protease inhibitors
Myopathic Syndromes

- Increased susceptibility with acute or chronic renal failure, obstructive liver disease and hypothyroidism
- Consider re-challenging or switching to another statin
- Pravastatin and fluvastatin - less muscle toxicity
CK elevation

- Other causes: hypothyroidism, trauma from athletics or high impact sports (running, hockey, etc)
- Discontinue statin if CK > 10 x ULN
- Consider switching statins
- Routine CK monitoring is not recommended
- Check baseline CK before statin therapy is initiated.
Renal Dysfunction

- Statins can cause proteinuria. Most reports are with Simvastatin and Rosuvastatin.
- Believed to be a benign finding
Memory Loss

• Review of adverse events reported to the FDA from 11/1997 – 2/2002 found 60 reports of memory changes. Most were with lipophilic statins (Atorvastatin and Simvastatin).

• Annals of Internal Medicine (2013) published a review of randomized trials and observational studies that did not suggest that statins harm cognition. Quality of evidence was low to moderate, especially with high-intensity therapy.
Prevention of Dementia

• Retrospective studies have shown that statins may prevent dementia.
• The Rotterdam study (n=6992) showed a decreased risk of Alzheimer's Disease.
• Randomized controlled trials with dementia or cognitive decline as a primary endpoint are needed to determine this risk.
Diabetes Mellitus

- Jupiter Trial, IDEAL, TNT, A to Z, PROVE IT – TIMI 22, SEARCH raised concern for new onset diabetes
- Increased incidence with higher dose statin therapy vs. moderate dose therapy
- One case DM for every 500 patients treated with intensive rather than moderate statin therapy
- Benefit of statins on cardiovascular events and mortality outweigh risks.
Pregnancy

• Category X
• Discontinue prior to conception
• Risk is likely small with statin use
  – Increase in congenital CNS and limb abnormalities with exposure of lipophilic statins in the 1\textsuperscript{st} trimester.
• Use discouraged while breastfeeding
Cancer

• 4S – 10 year follow up
• West of Scotland Coronary Prevention Study (WOSCOPS) – 10 year follow up
• Heart Protection Study (HPS) – 11 year follow up

Statins have no effect on cancer incidence or mortality
Cataracts

• Large cohort studies from England, Wales and US military health system found association of statins and increased cataracts

• Randomized trial in the British Journal of Ophthalmology (1995) showed no increase in risk of cataracts.
  – Most case control and cohort studies also support this.
Possible Risks

- Neuropathy – causal association with statin use
- Lupus – drug induced by statins
- Androgen synthesis
  - Men: Not clinically significant
  - Women: May reduce androgen levels
Special Populations
Chronic liver disease + statin

• Used to decrease cardiovascular risk
• Abstinence from alcohol
• Low dose Pravastatin (preferred)
• No increased risk with baseline aminotransferase elevation + statin
• Safe with Gilbert’s syndrome
• Primary biliary cirrhosis + Atorvastatin showed significant elevation in transaminases
  – Avoid statins with significant cholestasis
CKD + Statin

- Atorvastatin and Fluvastatin do not require dose adjustment in severe CKD
  - Pravastatin may be safer than other remaining options

- Dose adjustment is warranted with other statins with CrCl < 30 mL/min
Interactions

• CYP3A4: Cyclosporine, macrolide antibiotics, HIV protease inhibitors, CCB’s, Amiodarone, Antifungal agents
  – Grapefruit juice: 8-oz glass or one-half of a grapefruit or less is unlikely to cause a problem

• Fibrates: ex. Gemfibrozil, fenofibrate

• Niacin
NEW STATIN GUIDELINES

11/12/2013: New guidelines for cholesterol to reduce risk of ASCVD (atherosclerotic cardiovascular disease) in adults

Joint task force from the ACC (American College Of Cardiology) and AHA (American Heart Association)

12 years ago guidelines from ATP III- (Adult Treatment Panel, previous gold standard) with emphasis on LDL lowering for high risk patients
33,000 more people on STATINS!!!!

Cholesterol-lowering drugs

Third of all adults urged to take statins

Guidelines focus broadly on risks for heart, strokes

From staff and wire reports

The nation's first new guidelines in a decade for preventing heart attacks and strokes call for twice as many Americans — one-third of all adults — to consider taking cholesterol-lowering statin drugs.

The guidelines, issued Tuesday by the American Heart Association and American College of Cardiology, are a big change.

They use a new formula for estimating someone's risk that includes many factors besides cholesterol, the main focus now. They take aim at strokes, not just heart attacks. And they set a lower threshold for using medicines to reduce risk.

The definition of high cholesterol isn't changing, but the treatment goal is.

Instead of aiming for a specific number, using whatever drugs get a patient there, the advice stresses statins such as Lipitor and Zocor and identifies four groups of people they help the most.

“The emphasis is to try to treat more appropriately,” said Dr. Neil Stone, the Northwestern University doctor who headed the cholesterol guideline panel. “We’re going to give statins to those who are the most likely to benefit.”

Doctors say the new approach will limit how many people with low heart attack risks are put on statins simply because of a cholesterol number. Yet under the new advice, 33 million Americans — 44 percent of men and 22 percent of women — would meet the threshold to consider taking a statin. Under the current guidelines, statins are recommended for only about 15 percent of adults.
What’s known, what’s new

**KNOWN:**

• LDL matters- increased “bad” cholesterol leads to heart disease

**NEW:**

• 4 different “Statin Benefit Groups”:
• ID whose at the highest risk for having CVD and prescribe statin therapy
What’s different with new guidelines?

• Only evidence based randomized controlled trials used to provide the most compelling data

• New cardiovascular risk calculator

• Paradigm shift
4 Groups

- ACS (acute coronary syndrome)
- CAD, MI, CABG, stent
- PAD or history of arterial revascularization
- Stroke, TIA (new)
Statin Benefit Groups

• Whose with established ASCVD or established heart disease (secondary prevention)

• No history of heart disease, but LDL-C levels of >190 mg/dl or higher (primary prevention)

• Diabetics: 40-75 y/o with LDL 70-189 mg/dl without heart disease

• 40-75 y/o with LDL-C levels 70-189 with a 10 year risk of 7.5% or higher (no diabetes)
Not in the Recommended Group?

- Elevated high-sensitivity CRP 2 mg/L or higher - marker of inflammation
- Familial hyperlipidemia
- Family history – ASCVD onset in 1st degree male >55 or female >65
- Elevated coronary artery calcium score
- Elevated LP(a)
Guidelines Include:

• CAD
• STROKE
• PAD (peripheral arterial disease)
• DIABETES
Dislikes

• New risk assessment calculator to identify 10 year risk of CV disease likelihood - untested
• No recommendations for lowering triglycerides
• No benchmark for LDL goals
• Emphasis on high or moderate dose statins challenging with statin intolerance
2013 Risk Calculator

• The calculator uses nine pieces of information—sex, age, race, total cholesterol, HDL cholesterol, systolic blood pressure, current treatment for high blood pressure, diagnosis of diabetes, smoking habits.

• The new guidelines recommend a statin for seemingly healthy people with a risk of 7.5% or higher
“Something is terribly wrong,” Dr. Nissen said. Using the calculator’s results, he said, “your average healthy Joe gets treated, virtually every African-American man over 65 gets treated.”

- EMPHASIS ON AGE AND SEX. DOES NOT INCLUDE FAMILY HISTORY, TRIGS, CRP, LP(A)
65 year old male s/p MI at age 56, not active, no special diet

- TG : 365
- HDL-C : 35
- LDL-C : 78
- Glucose: :144

- What would you do first? Hint: new guidelines don’t address triglyceride levels
Average Jane

• 30 year old female, father died of MI at age 45
• total cholesterol of 270 mg/dL
• Triglycerides: 360 mg/dL
• HDL- 45
• LDL-180

• Due to her young age, risk calculator doesn’t apply. Should we wait 10 years to treat??
65 y/o AA male, primary prevention, no history of CAD, DM, HPTN. LP(a) normal.

Fasting lipids:
Total cholesterol 190 mg/dL
HDL: 64
Triglycerides: 125
LDL-76
BP 130 systolic

New calculator: 10 year risk score of CV disease= 7.5%
Recommend moderate intensity statin treatment (overtreatment)
Do I really need a statin? Individualize!
All Statins are NOT Created Equal

• **Generic:**
  - Pravastatin (gentle)
  - Simvastatin (restrictions past 40 mg)
  - Atorvastatin (lipitor)

• **Not Generic:**
  - Rosuvastatin (crestor)
  - Pitavastatin
## Lipophilic vs. Hydrophilic statins

<table>
<thead>
<tr>
<th>Statin Name</th>
<th>Dosing Details</th>
<th>Hydrophility</th>
<th>Enzyme Metabolized</th>
<th>Dosing Options</th>
</tr>
</thead>
</table>
| Atorvastatin (Lipitor) | 10 mg: 35-39%  
20 mg: 43%  
40 mg: 50%  
80 mg: 55-60% | Lipophilic | Extensive CYP3A4 | 10-40 mg: Moderate  
80 mg: High |
| Atorvastatin/ezetimibe (Liptruzet) | 10/10 mg: 53%  
20/10 mg: 54%  
40/10 mg: 56%  
80/10 mg: 61% | Lipophilic | Extensive CYP3A4 | 10-40 mg: Moderate  
80 mg: High |
| Fluvastatin (Lescol, Lescol XL) | 20 mg: 22%  
40 mg: 25%  
80 mg: 35% (XL product) | Lipophilic | Extensive CYP2C9, CYP3A4 | 20-40 mg: Low  
40 mg BID: Moderate  
80 mg XL: Moderate |
| Lovastatin (Mevacor) | 10 mg: 21%  
20 mg: 24-27%  
40 mg: 30-31%  
80 mg: 40-42% | Lipophilic | Extensive CYP2C9, CYP3A4 | 20 mg: Low  
40 mg: Moderate |
| Pitavastatin (Livalo) | 1 mg: 31-32%  
2 mg: 36-39%  
4 mg: 41-45% | Lipophilic | Glucuronidation  
Marginal CYP2C9 | 1 mg: Low  
2-4 mg: Moderate |
| Pravastatin (Pravachol) | 10 mg: 22%  
20 mg: 32%  
40 mg: 34%  
80 mg: 37% | Hydrophilic | Extensive Sulfation | 10-20 mg: Low  
40-80 mg: Moderate |
| Rosuvastatin (Crestor) | 5 mg: 45%  
10 mg: 46-52%  
20 mg: 47-55%  
40 mg: 55-63% | Hydrophilic | Minor CYP2C9 | 5-10 mg: Moderate  
20-40 mg: High |
| Simvastatin (Zocor) | 5 mg: 26%  
10 mg: 30%  
20 mg: 38%  
40 mg: 29-41% | Lipophilic | Unknown | Extensive CYP3A4 |

*If CrCl < 30, use doses over 20 mg daily with caution*
Preventive Cardiology Jb-1

• Clear LDL goals: may be as high as 130 mg/dL or as low as 70 mg/dL
• Lifestyle management is addressed: diet, weight, exercise, co-morbidities, risk factors
  - start statin lowest dose and increase as tolerated
**LDL Levels Among Statin-Intolerant Adults**

Patients referred to the prevention clinic who could not tolerate statins still experienced reductions in LDL levels. Patients had at least two follow-up visits within a year.

**Primary Prevention, Statin-Intolerant Adults (N = 152 in 2012)**

2007 – 2012

**Secondary Prevention, Statin-Intolerant Adults (N = 135 in 2012)**

2007 – 2012
Statin Intolerance

• Literature suggests statin related events 5-10% in RCT
• Clinical practice: 20% or more of patients experience subjective intolerance
• Muscle aches, weakness, constant, often bilateral. Symptoms relieved within days after stopping statins
Therapies for statin intolerance

- Co-enzyme Q-10
- Treating vitamin D deficiency
- Switching statins
- Adding non-statin therapy
- Drug holiday- re-challenge
# Statin Dose Equivalency

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Fluvastatin</th>
<th>Pravastatin</th>
<th>Lovastatin</th>
<th>Simvastatin</th>
<th>Atorvastatin&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Rosuvastatin&lt;sup&gt;a&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1</td>
<td>20 mg</td>
<td>20 mg</td>
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<td>5–10 mg</td>
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<td>6&lt;sup&gt;b&lt;/sup&gt;</td>
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<sup>a</sup>The following agents were defined as branded at the time of this analysis.

<sup>b</sup>Level 6 consists of levels 6 and 7 from the published algorithm.
**Dose Conversion Table for Statins:**

<table>
<thead>
<tr>
<th>% LDL Reduction</th>
<th>LOVASTATIN (MEVACOR)</th>
<th>PRAVASTATIN (PRAMACHOL)</th>
<th>SIMVASTATIN (ZOCOR)</th>
<th>LESCOL (40MG)</th>
<th>LIPITOR</th>
<th>CRESTOR</th>
<th>VYTORIN</th>
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<tbody>
<tr>
<td>25-32%</td>
<td>20MG</td>
<td>20MG</td>
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<tr>
<td>33-49%</td>
<td>40MG</td>
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<tr>
<td>48-52%</td>
<td>80MG</td>
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<td>55-60%</td>
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<td>60-63%</td>
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</table>

*TRADE NAMES WITH AEQUIVALENT GENERICS AVAILABLE*

- **White Zone**: Available Generically
- **Black Zone**: Brands that have dose equivalent generics available – WILL require patient to try a generic before covered
- **Dark Gray Zone**: Brands that have only high-dose generic alternative available – WILL NOT require patient to try a generic for coverage
- **Light Gray Zone**: Brands that have no equivalent generics available – WILL NOT require patient to try a generic for coverage

 portfolios, and other documents. Do not hallucinate.
Caution: FDA warning

- **Simvastatin:** limit dosing to no more than 40 mg daily.
- No more than 10 mg simvastatin if patient on amiodarone, diltiazem, verapamil: FDA alert 2011 (considered low dose statin) due to risk of myopathy.
- **Amlodipine, ranexa:** no more than simvastatin 20 mg.
- **Simva contraindicated:** antifungal –azole, antimicrobials –mycins, HIV protease inhibitors.
Intermittent dosing

Rosuvastatin (Crestor) in particular can effectively be dosed as low as 2.5 mg twice weekly due to:

– Long half-life

– High potency
72 y/o male with CAD tolerated atorvastatin for > 3 years before progressive muscle fatigue

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<tbody>
<tr>
<td>CK</td>
<td>30 - 220 U/L</td>
<td>3283 (H)</td>
<td>2957 (H)</td>
<td>2899 (H)</td>
<td>2293 (H)</td>
<td>1915 (H)</td>
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CK elevation

- While on statins if CK > 2.5 times normal stop the statin and monitor symptoms

If CK back down to normal after stopping statin, can re-challenge with different drug or dose
Cleveland Clinic Experience

• PC analyzed EMR of 1,605 patients with documented intolerance to at least two statins (between 1995-2010)
• Study showed most patients can tolerate some statin as opposed to none at all
3 groups analyzed

Daily statins, intermittent statin, no statin use

LDL lowering and all cause mortality analyzed

Trend toward a survival benefit for those who could tolerate some statin vs. no statin group
An Apple A Day?

• 150 year old proverb has withstood the test of time

• Apple + statin to >50 age group for primary prevention in the UK theorized

• BMJ 2013: 347, p. 1-6
It’s Complicated:

• 3/14/2014 YouTube Dr. Oz
Apple vs. Statin
References

References


• Ridker, PM, Danielson, MIA, Fonceca, FAH, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. NEJM 359; 2159-2207.


