Hyperlipidemia: Update on Guidelines and Emerging Therapies

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The speaker has no actual or potential conflicts of interest related to this presentation
Objectives

- Describe cardiovascular benefit of reducing low-density lipoprotein (LDL)
- Discuss current guideline recommendations for hyperlipidemia treatment
- Identify patients who may benefit from additional lipid-lowering therapy
Cardiovascular Disease (CVD)

- Low-density lipoprotein (LDL) is a known CV risk factor
- Risk includes myocardial infarction, coronary heart disease, and ischemic stroke

Benefits of Lowering LDL

Every 38.7 mg/dL drop in LDL

22% relative risk reduction in CV events

Current Guidelines

AHA/ACC
- Eliminated lipid targets
- Recommends statins for specific groups

NLA
- Non-HDL and LDL goals of <100mg/dL and <70mg/dL respectively
- Non-statin treatment if not at goal

AHA/ACC:
States “non-statin therapies do not provide acceptable ASCVD benefit relative to their potential side effects”

ACC ECDP

• Recommends clinicians to consider additional non-statin therapy if:
  - Patient has not achieved ≥ 50% reduction in LDL
  - LDL > 70 mg/dL or non-HDL > 100 mg/dL in patients with diabetes on maximum tolerated statin

• Decision pathway would then recommend:
  - Consider ezetimibe first
  - Consider adding or replacing with PCSK9 inhibitor second
Treatment

• Statins
  - First-line therapy
  - HMG-CoA reductase inhibitors
  - Do not use in liver failure
  - Side effect: myalgias

• Ezetimibe (Zetia®)
  - Inhibits intestinal absorption of cholesterol
  - Adding to statin therapy could decrease LDL by up to 20%

Treatment- PCSK9 inhibitors

• Drugs
  - Alirocumab (Praluent®)
  - Evolocumab (Repatha®)

• Side effects
  - Injection site reactions
  - Upper respiratory symptoms
  - Cost

Annual cost of lipid lowering therapy:
  Statin: $186
  Praluent®: $14,600

Treatment- PCSK9 inhibitors

FOURIER

<table>
<thead>
<tr>
<th>Site:</th>
<th>Multinational including 1,242 sites in 49 countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population:</td>
<td>27,564 patients with ASCVD, LDL ≥ 70 mg/dL, and on a statin</td>
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<tr>
<td></td>
<td>81% had a history of MI</td>
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<tr>
<td></td>
<td>69% on high-intensity statin and 30.4% on moderate-intensity statin</td>
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<tr>
<td>Intervention:</td>
<td>Placebo versus evolocumab 140 mg Q 2weeks or 420 mg monthly</td>
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<td>Median duration follow up was 26 months</td>
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</table>

## FOURIER- Results

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Evolocumab</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LDL at 160 weeks</strong></td>
<td>86 mg/dL</td>
<td>33 mg/dL</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Cumulative incidence of MI, stroke, or death at 36 months</strong></td>
<td>11.3%</td>
<td>9.8%</td>
<td>&lt;0.001</td>
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</tbody>
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## FOURIER - Adverse Effects

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Placebo (%) n = 13,756</th>
<th>Evolocumab (%) n = 13,769</th>
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<tbody>
<tr>
<td>Serious</td>
<td>3,404 (24.7)</td>
<td>3,410 (24.8)</td>
</tr>
<tr>
<td>Injection site reaction**</td>
<td>219 (1.6)</td>
<td>296 (2.1)</td>
</tr>
<tr>
<td>Muscle-related event</td>
<td>656 (4.8)</td>
<td>682 (5.0)</td>
</tr>
<tr>
<td>Cataract</td>
<td>242 (1.8)</td>
<td>228 (1.7)</td>
</tr>
<tr>
<td>Neurocognitive event</td>
<td>202 (1.5)</td>
<td>217 (1.6)</td>
</tr>
</tbody>
</table>

Conclusions

Proven cardiovascular benefit in reducing LDL

LDL reduction can lead to improved CV outcomes with minimal side effects

Additional non-statin therapy may be needed for those intolerant to or not achieving goal with statins
Learning Assessment Question 1

What is the CV event relative risk reduction for every 38.7 mg/dL decrease in LDL?

A. 50%
B. 34%
C. 22%
D. 12%
Which of the following is true regarding hyperlipidemia LDL goals from the 2013 AHA/ACC guideline?

A. LDL goal of <120 mg/dL
B. LDL goal of <100 mg/dL
C. LDL goal of <70 mg/dL
D. No LDL level goal