Advances in the Treatment of Hyperlipidemia

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Objectives for Lecture

• At the conclusion of the lecture, the successful learner will be able to:
  – Select the LDL goal given specific patient characteristics
  – Select the appropriate first and adjunctive therapies for patients with differing patient profiles
  – Identify the clinical trial and pharmacoconomic results that drove these guideline recommendations
  – Apply knowledge of drugs to construct adequate patient monitoring plans and mitigate adverse events
ASCVD = ACS, stable angina, arterial revascularization, stroke/TIA, PAD, aortic aneurysm

Very High Risk = 2 or more Column A [or] 1 from Column A and Multiple From Column B

<table>
<thead>
<tr>
<th>Major ASCVD Events</th>
<th>High-Risk Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent ACS (within the past 12 mo)</td>
<td>Age ≥65 y</td>
</tr>
<tr>
<td>History of MI (other than recent ACS event listed above)</td>
<td>Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe</td>
</tr>
<tr>
<td>History of ischemic stroke</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Symptomatic PAD (claudication with ABI &lt;0.85, previous revascularization/amputation)</td>
<td>History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)</td>
</tr>
<tr>
<td>Heterozygous familial hypercholesterolemia</td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>CKD (eGFR 15-59 mL/min/1.73 m)</td>
</tr>
<tr>
<td></td>
<td>Current smoking</td>
</tr>
<tr>
<td></td>
<td>History of congestive HF</td>
</tr>
</tbody>
</table>

Grundy S. JACC 2018; https://doi.org/10.1016/j.jacc.2018.11.003
AHA/ACC Risk Calculator

http://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp then click on web based risk calculator in upper right.
For High or Very High Risk

- Regardless of the LDL goal, should get a 50% reduction in LDL from baseline
  - For example, someone with an LDL of 100mg/dL before their MI should get at least a 50% reduction even though this reduction will give the patient an LDL of 50mg/dL

Grundy S. JACC 2018; https://doi.org/10.1016/j.jacc.2018.11.003
## Lipid Lowering Drugs and Potencies

### Prescription Adjunct Agents

**Lipid Impact**

<table>
<thead>
<tr>
<th>Drug</th>
<th>LDL Impact</th>
<th>TG Impact</th>
<th>HDL Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Apheresis</td>
<td>-50 to -68%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Statins</td>
<td>-35 to -58%</td>
<td>-10 to +25%</td>
<td>+7 to +12%</td>
</tr>
<tr>
<td>PCSK9 Inhibitors</td>
<td>-35 to -58%</td>
<td>-5 to -15%</td>
<td>+4 to +6%</td>
</tr>
<tr>
<td>Lomitapide</td>
<td>-30 to -40%</td>
<td>-40 to -50%</td>
<td>-7%</td>
</tr>
<tr>
<td>Mipomerson</td>
<td>-25%</td>
<td>-18%</td>
<td>+15%</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>-15 to -20%</td>
<td>-5 to -8%</td>
<td>+3 to +5%</td>
</tr>
<tr>
<td>BAS</td>
<td>-15 to -20%</td>
<td>0 to -10%</td>
<td>+3 to +5%</td>
</tr>
<tr>
<td>Niacin</td>
<td>-15 to -20%</td>
<td>-20 to -50%</td>
<td>+15 to +35%</td>
</tr>
<tr>
<td>Fibric Acid Deriv</td>
<td>-10 to +10%</td>
<td>-30 to -60%</td>
<td>+9 to +20%</td>
</tr>
<tr>
<td>Omega-3 FAs</td>
<td>-5 to +44%</td>
<td>-30 to -60%</td>
<td>+5 to +10%</td>
</tr>
</tbody>
</table>

Natural Products With Evidence to Show Benefits in LDL and Triglyceride Lowering (Niacin and Omega-3 Not Included Due to FDA Indication)

**Table 3: Natural Products for Cholesterol Reduction**

<table>
<thead>
<tr>
<th>Active substance</th>
<th>LDL</th>
<th>TG</th>
<th>HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red yeast rice</td>
<td>-35.0 mg/dL*</td>
<td>-25.6 mg/dL</td>
<td>+3.6 mg/dL</td>
</tr>
<tr>
<td>Soluble fiber</td>
<td>-10.2* to -16.0 mg/dL*</td>
<td>-11.1* to -11.8 mg/dL*</td>
<td>-1.4 to +1.0 mg/dL</td>
</tr>
<tr>
<td>Sterols and stanols</td>
<td>-12.2 mg/dL*</td>
<td>-5.1 mg/dL</td>
<td>+2.14 mg/dL</td>
</tr>
<tr>
<td>Cinnamon</td>
<td>-9.4 mg/dL*</td>
<td>-29.6 mg/dL*</td>
<td>+1.7 mg/dL*</td>
</tr>
<tr>
<td>Almonds</td>
<td>-5.8 mg/dL</td>
<td>-1.7 mg/dL</td>
<td>-1.8 mg/dL</td>
</tr>
<tr>
<td>Green tea extract</td>
<td>-5.3 mg/dL*</td>
<td>-3.0 mg/dL</td>
<td>-0.27 mg/dL</td>
</tr>
<tr>
<td>Garlic</td>
<td>-2.3 mg/dL</td>
<td>-4.2 mg/dL*</td>
<td>+1.0 mg/dL</td>
</tr>
</tbody>
</table>

*Indicates that statistical significance was not reached in trials evaluating efficacy.

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides

Guideline Approved Statins

<table>
<thead>
<tr>
<th>High Intensity</th>
<th>Moderate Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL Reduction &gt;50%</td>
<td>LDL Reduction 30-50%</td>
</tr>
<tr>
<td>Atorvastatin 40-80mg</td>
<td>Atorvastatin 10-20mg</td>
</tr>
<tr>
<td>Rosuvastatin 20-40mg</td>
<td>Rosuvastatin 5-10mg</td>
</tr>
<tr>
<td>Simvastatin 20-40mg</td>
<td>Pravastatin 40-80mg</td>
</tr>
<tr>
<td>Lovastatin 40mg</td>
<td>Pitavastatin 2-4mg</td>
</tr>
<tr>
<td>Fluvastatin 40mg BID</td>
<td></td>
</tr>
</tbody>
</table>

Grundy S. JACC 2018; https://doi.org/10.1016/j.jacc.2018.11.003
# Guideline Approved Adjuncts

<table>
<thead>
<tr>
<th>20% Reduction to Goal</th>
<th>Ezetimibe</th>
<th>Ezet + BAS</th>
<th>PCSK9 Inh</th>
</tr>
</thead>
<tbody>
<tr>
<td>++ + + + +</td>
<td>Effective, safe, well tolerated, low cost, proof of event reductions</td>
<td>Impossible to have cost/QALY &lt; $100,000/year</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>35% Reduction to Goal</th>
<th>Ezetimibe</th>
<th>Ezet + BAS</th>
<th>PCSK9 Inh</th>
</tr>
</thead>
<tbody>
<tr>
<td>++</td>
<td>Effective, safe, well tolerated, low cost BUT no proof of benefits over ezet alone</td>
<td>++</td>
<td>Effective, safe, well tolerated, proof of event reduction BUT very high cost</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>50% Reduction to Goal</th>
<th>Ezetimibe</th>
<th>Ezet + BAS</th>
<th>PCSK9 Inh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower NNTs Help with Cost-Effectiveness</td>
<td>++ + + + +</td>
<td>Effective, safe, well tolerated, proof of event reduction BUT very high cost</td>
<td></td>
</tr>
</tbody>
</table>


# Landmark Clinical Trials

Research Drives Guidelines
Statin vs. Placebo: Landmark Clinical Trials

• Primary Prevention: WOSCOPS, AFCAPS/TexCAPS, ASCOT-LLA, JUPITER
  – Prava, lova, atorva, rosuva reduce cardiac events
• Secondary prevention: CARE, LIPID, 4S, HPS, GREACE
  – Prava, simva, atorva reduce mortality and recurrent events


LDL-C Lowering With Statins: Reduced CHD Events

High vs. Low Intensity Statins: Landmark Clinical Trials

- Secondary Prevention Trials
  - PROVE-IT Trial
    - Prava 40mg vs Atora 80mg
    - LDL 90-100mg/dL vs. 60-70mg/dL
  - TNT Trial
    - Atorva 10mg vs. Atorva 80mg
    - LDL 90-100mg/dL vs. 60-70mg/dL
- LOWER LDL IS BETTER


### PROVE-IT: Final Health Outcomes

<table>
<thead>
<tr>
<th>Primary end point</th>
<th>Pravastatin 40 mg (n=1973)</th>
<th>Atorvastatin 80 mg (n=2003)</th>
<th>Relative risk reduction, %</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, MI, UA, PCI, CABG, Stroke</td>
<td>26.3%</td>
<td>22.4%</td>
<td>16%</td>
<td>0.005</td>
</tr>
<tr>
<td>Secondary end points</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>3.2%</td>
<td>2.2%</td>
<td>28%</td>
<td>0.07</td>
</tr>
<tr>
<td>Revascularization</td>
<td>18.8%</td>
<td>16.3%</td>
<td>14%</td>
<td>0.04</td>
</tr>
</tbody>
</table>

## Adjunct Trials w/ Additional LDL Lowering

<table>
<thead>
<tr>
<th>Variables</th>
<th>IMPROVE-IT 2014</th>
<th>FOURIER 2018</th>
<th>ODYSSEY OUTCOMES 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy</td>
<td>Ezet 10mg + Simva 40mg vs. Plac + Simva 40mg</td>
<td>Evolocumab 140mg Q2W or 420mg QM vs. Plac</td>
<td>Alirocumab 75mg or 150mg Q2W vs. Plac</td>
</tr>
<tr>
<td>Inclusion Criteria</td>
<td>Everyone needed to be on moderate to max statins</td>
<td>Pts w/ Hx of MI, Stroke, PAD</td>
<td>Pts &lt;1y post ACS</td>
</tr>
<tr>
<td>Population</td>
<td>Pts &lt; 10 days of ACS</td>
<td>Pts w/ Hx of MI, Stroke, PAD</td>
<td>Pts &lt;1y post ACS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>6 y</td>
<td>2 y</td>
<td>4 y</td>
</tr>
<tr>
<td>LDLs Baseline</td>
<td>94mg/dL, E:53; P:70mg/dl</td>
<td>94mg/dL, E:30; P:92mg/dL</td>
<td>93mg/dL, A:53.3; P:101mg/dL</td>
</tr>
<tr>
<td>% Diff LDL</td>
<td>-24%</td>
<td>-67%</td>
<td>-55%</td>
</tr>
</tbody>
</table>


## Adjunct Trials w/ Additional LDL Lowering

<table>
<thead>
<tr>
<th>Variable</th>
<th>IMPROVE IT</th>
<th>ODYSSEY Outcomes</th>
<th>FOURIER</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE Events</td>
<td>35% vs. 33%, P=0.016</td>
<td>11.1% vs. 9.5%, P&lt;0.001</td>
<td>11.0% vs. 9.2%, P&lt;0.001</td>
</tr>
<tr>
<td>Death</td>
<td>15% vs. 15% P=0.782</td>
<td>4.1% vs. 3.5%, P=0.023</td>
<td>3.2% vs. 3.1%, P=0.99</td>
</tr>
<tr>
<td>MI</td>
<td>18% vs. 13%, P=0.002</td>
<td>7.6% vs. 6.6%, P=0.006</td>
<td>4.6% vs. 3.4%, P&lt;0.01</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>4.1% vs. 3.4%; P=0.008</td>
<td>1.6% vs. 1.2%, P=0.01</td>
<td>1.9% vs. 1.5%, P=0.01</td>
</tr>
<tr>
<td>Revasc Proc</td>
<td>23% vs. 22% P=0.107</td>
<td>8.8% vs. 7.7%, P=0.009</td>
<td>7.0% vs. 5.5%, P&lt;0.01</td>
</tr>
</tbody>
</table>
**LDL-CV Event Reduction Relationship**

- Cholesterol Treatment Trialists (CTT) assessment of all major statin vs. placebo, statin vs. statin, and statin + adjunct ezetimibe or PCSK9 inhibitor vs. statin trial
- For every 39mg/dL reduction in LDL, the 5-year risk of cardiovascular events is reduced by 22%
  - Holds for LDL’s as low as 30mg/dL


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**Not Everyone Should have an LDL of 30mg/dL**

- If 50 of 100 of people over 5 years will have an ASCVD event, reducing that risk by 50% prevents 25 events
- If 10 of 100 people over 5 years will have an ASCVD event, reducing it by 50% prevents 10 events
  - 1/ARR = NNT
- NNT = number needed to treat to prevent one event
NNTs for Different Patients To Reduce one Cardiovascular Event


PCSK9 Cost Effectiveness

- In an analysis, the cost-effectiveness of the PCSK9 inhibitors was estimated
- If the NNT on PCSK9 inhibitor therapy is 30 to 50, 15 to 29, or 10 to 14, therapy would cost ~$300 000, ~$280 000, or ~$150 000 per quality adjusted life year (QALY) at $14,000 per year
  - Currently priced at $6,000, PCSK9 with an NNT of 30-50 would be reasonably cost effective (~$64,285 per QALY)

Statin + HDL Increasing Adjunctive Therapy

- Adjunctive therapies improve lipid effects over statins alone
- Therapy to raise HDL
  - Niacin + Simva vs. Simva alone (AIM-HIGH, HPS-THRIVE)
  - Fenofibrate + Statin vs. Statin alone (ACCORD)
  - CETP Inhibitors + Statin vs. Statin Alone (ILLUMINATE)
  - Combo does not impact final cardiovascular health outcomes (death, MI, ACS, stroke, revascularization)
  - These drugs had little to no LDL lowering and niacin trials had high withdrawal rates

White CM. Drug Topics 2014;2:53-60
Drug Therapy: Statins

- **Contraindications**
  - Pregnancy, breastfeeding (category X)
  - Active liver disease or high unexplained liver transaminases (AST, ALT, LDH)
    - Fatty liver can raise liver transaminases and statins don’t worsen it (and may help treat it)
    - LFTs checked at baseline and when clinically indicated
      - If baseline LFT >3X ULN, find out reason
      - Normal: AST 0-35mg/dL, ALT 5-40mg/dL, LDH 50-150mg/dL
      - If any follow-up LFT >3X ULN, hold statin until resolution and reinitiate with another statin, lower the dose, or use another class
      - No resolution of LFT elevation, liver biopsy
  - Pravastatin, rosuvastatin, simvastatin has lower risk of LFT elevation/hepatotoxicity than atorvastatin
  - Greater risk with concurrent fibrate or niacin use


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**Persistent ALT > 3 × ULN Frequency by % LDL-C Reduction**

![Graph showing various statins and their percentage of persistent ALT > 3 × ULN at different LDL-C reductions](image)

Ref: Prescribing Information and Summary Basis of Approval documents.
Proteinuria

• Incidence 1.1% rosuvastatin vs. 0.4% other statins
• Excretion of α-1 & β-2 microglobulin, not albumin
  – Reduced reabsorption of small proteins usually reabsorbed in kidney tubules
• If hematuria (blood in urine), halt statin therapy til resolved and switch to another statin or another class

Muscle Toxicity

• Myalgia
  – Muscle pain
    • Test CK (normal 10-150u/L Male 10-130u/L Female)
      – If CK in myopathy range >10X ULN (1300u/L female, 1500u/L male), stop therapy
      – If >3X ULN, stop therapy or test weekly til 10X ULN or normalization
• Rhabdomyolysis
  – Seldom occurs without myalgia preceding it
    • Counsel to contact physician if myalgia, especially with fever and malaise
  – Severe muscle breakdown
  – Myoglobinemia and myoglobinuria common
    • Brownish or black urine
  – Can cause renal failure
  – Can cause prolonged muscle weakness needing rehabilitation
• Greater risk of rhabdomyolysis with simvastatin and lovastatin than hydrophilic statins (atorvastatin, pravastatin, fluvastatin, rosuvastatin, pitavastatin)
• Greater risk with concurrent fibrate, daptomycin, colchicine, niacin or for simvastatin, lovastatin, atorvastatin the use of CYP3A4 inhibitors

AHFS 2001, FDA NDAC Advisory Panel (7/13/00 from www.FDA.gov)
Why Muscle Toxicity?

HMG CoA Reductase

HMG CoA

Mevalonate

Isopentenyl Pyrophosphate

Geranyl Pyrophosphate

Farnesyl Pyrophosphate

Squalene

Dihydro Ubiqunone

Cholesterol

Future Products Involved in Protein Synthesis

Future Products Involved in Signal Transduction

Ubiquinone Involved in Cellular Metabolism

Needed for Membrane Stability


Intra-Muscle IC50 for Synthesis

![Bar chart showing protein and ATP levels with different drugs]

Metabolic Pathways & Rhabdomyolysis

- Lova, sima, and atorva are CYP3A4 substrates
  - Inhibitors of CYP 3A4 increase risk of rhabdomyolysis
  - Lower risk with atorva
- Lova and simva are contraindicated with potent CYP3A4 inhibitors & Lova, Simva, and Atorva have maximum dosing limits with CYP3A4 inhibitors (see PIs)
- CYP3A4 inhibitors: Azole antifungals (ketoconazole, itraconazole), macrolides (erythromycin, clarithromycin, trandeolamycin), cyclosporin, nefazodone, nondihydropyridine CCBs (diltiazem, verapamil), protease inhibitors (saquinavir, indinavir, ritonavir, amprenavir), amiodarone, dronedarone
- 93% of simva/lova rhabdomyolysis cases occur w/ concurrent CYP3A4 inhibitors

Drug PIs.

Diltiazem + Lovastatin
High Variability in Interaction Magnitude

Lovastatin AUC (% control)

Statin/Fibrate Combinations

Hydroxysimvastatin
Hydroxyacid
Lactone
Simvastatin

5.6 2.9 2.8
2.0 1.9

Cerivastatin
Simvastatin acid
Lovastatin acid
Pravastatin
Rosuvastatin

AUC ratio

Effect of Gemfibrozil on Statin Plasma Concentrations

Ratio of AUC in gemfibrozil-treated patients to AUC in placebo patients

Effect of Gemfibrozil and Fenofibrate on Rosuvastatin Plasma Concentrations

Ratio of rosuvastatin AUC in fibrate-treated patients to AUC in placebo-treated patients

- **Gemfibrozil**: AUC ratio of 1.90
- **Fenofibrate**: AUC ratio of 1.07

Pitavastatin

- Normal doses 1-4mg
- Substrate for Uridine Diphosphate Glucuronosyltransferase (UGT)
  - Pitava contraindicated with cyclosporin
  - Max dose 2mg with rifampin
  - Max dose 1mg with erythromycin
  - Ataznavir, lopinavir, ritonavir have minor interaction
Dosing Pearls: Absorption

• Bioavailability of lovastatin ↑ 50% by food
  – High fiber meals reduce bioavailability
  – Dose with dinner for most food with least fiber
• Can’t use lovastatin with bile acid sequestrants
  – Both need dosing with meals


Dosing Pearls: Half-Life

• Short half-life drugs (fluvastatin, pravastatin) should optimally be dosed QHS
  – This is because night is the optimal time for circadian activation of HMG CoA reductase
• Others can be dosed at any time

<table>
<thead>
<tr>
<th>Drug</th>
<th>Use in Renal Dx</th>
<th>Pregnancy/Breastfeeding</th>
<th>Drug Intx</th>
<th>GI ADEs</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Niacin</td>
<td>Use Caution</td>
<td>Pregnancy: Cat C Breastfeed: Possible Use</td>
<td>None</td>
<td>+++ Dyspepsia, Nausea, Contraind with PUD</td>
<td>1. ↑ Uric Acid and Transient Serum Glucose Conc 2. False + for catecholamines or glucose in urine</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>Yes</td>
<td>Pregnancy: Cat C Breastfeed: Possible Use</td>
<td>Ezet + Feno = Increased Gallbladder Risk Ezet ↑ Cyclosporin</td>
<td>+ Diarrhea</td>
<td>1. Only one dose (10mg) 2. Not Recommended in ↓ LFTs but not Contraind</td>
</tr>
<tr>
<td>PCSK9 Inh</td>
<td>Yes, No Data in Severe Dx</td>
<td>Pregnancy: No Data Breastfeed: No Data</td>
<td>No known drug intx</td>
<td>No adverse GI effects</td>
<td>SQ dosing (q2 or 4 weeks) Injection site irritation Immunogenicity potential Possible neurocognitive ADEs</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Use in Renal Dx</th>
<th>Pregnancy/Breastfeeding</th>
<th>Drug Intx</th>
<th>GI ADEs</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lomitapide</td>
<td>Yes</td>
<td>Pregnancy: Cat X Breastfeed: Do not use</td>
<td>Contra w/ CYP3A4 inh, Blocks CYP3A4 and PGP</td>
<td>++++ Diarrhea, Nausea, Flatulence</td>
<td>1. Supplement Fat Soluble Vits 2. Can Raise LFTs</td>
</tr>
<tr>
<td>Mipomerson</td>
<td>No use in Severe Renal Dx, Dialysis, Proteinuria</td>
<td>Pregnancy: Cat B Breastfeed: Use Caution</td>
<td>None</td>
<td>No</td>
<td>1. SQ Dosing Only 2. No Use in Fatty Liver Dx</td>
</tr>
</tbody>
</table>
Conclusions

- LDL is bad cholesterol, increases ASCVD risk
- Given the NNT, there are individual LDL targets for people based on baseline risk
- Statins are first line therapy to achieve LDL goals
  - Maximize statin dose or switch between statins before leaving statin class or using adjunctive therapy
  - Ezetimibe and PCSK9 Inhibitors are the best studied adjuncts to statins if additional LDL is needed
    - Role of bile acid sequestrants unproven for event reduction, niacin does not provide additional benefits
Conclusions

• Simva, lova, atorva are CYP3A4 substrates and pitava is a UGT substrate
  – Myriad of inhibitors that increase muscle risk
• Counsel on statin muscle symptoms and check CK when symptoms arise
  – Warnings if CK is >3X ULN, DC if ≥10X ULN
• Three statins have targeted ingestions times
  – Lova at dinner, prava and fluva at bedtime

Conclusions

• PCSK9 inhibitors are new, expensive, potent LDL reducers
• Ezetimibe is not as potent but cheaper than PCSK9s
• Each drug class has monitoring parameters and counseling points that should be communicated to patients
• Drug within a class have features that differentiate it from the others, knowing those features empowers you to be the drug expert
Questions?

Hypertriglyceridemia Therapy
Hypertriglyceridemia Risks

• Hypertriglyceridemia diagnosis made on fasting triglyceride levels only


<table>
<thead>
<tr>
<th>Table 17 Possible causes of hypertriglyceridaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic predisposition</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>Diet high in simple carbohydrates</td>
</tr>
<tr>
<td>Renal disease</td>
</tr>
<tr>
<td>Hypothyroidy</td>
</tr>
<tr>
<td>Pregnancy (physiological triglyceride</td>
</tr>
<tr>
<td>concentrations double during the third</td>
</tr>
<tr>
<td>trimester)</td>
</tr>
<tr>
<td>Paraproteinemia and autoimmune disorders</td>
</tr>
<tr>
<td>such as systemic lupus erythematosus</td>
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</tbody>
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Hypertriglyceridemia Risks

• Medications that can cause hypertriglyceridemia/pancreatitis: A TV FEAST PAPA, I ACT

<table>
<thead>
<tr>
<th>A TV</th>
<th>FEAST</th>
<th>PAPA</th>
<th>I ACT</th>
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</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Furosemide</td>
<td>Pentamidine</td>
<td>Isotretinoin</td>
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<tr>
<td>Tetracyclines</td>
<td>Estrogens</td>
<td>Atypical Antipsychotics</td>
<td>Antiretrovirals</td>
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<tr>
<td>Vaproic Acid</td>
<td>Azathioprine</td>
<td>Propafol</td>
<td>Cyclosporin</td>
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<tr>
<td>Steroids (cortico/anabolic)</td>
<td>Asperagenase</td>
<td>Tamoxifen</td>
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<td>Thiazides</td>
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Hypertriglycerideridemia Therapy

- Diet and exercise to achieve weight reduction, limit simple carbohydrates (sugar, starch, beer, wine)
- Statins are first line if LDL goal not met and triglycerides <500mg/dL
- Fibrates are first-line therapy if triglycerides >500mg/dL
  - Fibrates, niacin, or omega-3 fatty acids alone or in combination with statins are alternatives
  - Statins are not monotherapy in patients with severe or very severe hypertriglycerideridemia

Berglund L. J Clin Endocrinol Metab 2012; 97:2969.
Omega-3 FAs

• Dosing
  – 2-4g for triglyceride reduction

• Main ADEs
  – Dyspepsia
  – Burping fish oil smell
  – Nausea
  – Diarrhea

ESC 2016: Lifestyle Modifications