PCSK9 Inhibitors: Impact on the Management of LDL Apheresis Candidates and LDL Apheresis Patients

Anne Carol Goldberg, MD, FNLA
Professor of Medicine
Washington University School of Medicine
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Disclosure

- Board and committee membership—National Lipid Association, Foundation of National Lipid Association

- Guideline development—ACC/AHA 2013 Cholesterol Guideline, Endocrine Society Triglyceride Clinical Practice guideline, National Lipid Association Familial Hypercholesterolemia Recommendations

- Research contracts—Merck, Genzyme/ISIS, Genzyme/Sanofi-Aventis, Glaxo-Smith-Kline, Regeneron/Sanofi-Aventis, Amarin, Amgen, Pfizer, IONIS, Regeneron, Genentech/Roche (all grants to medical school)

- Consulting—Sanofi-Aventis, OptumRx

- Editorial—Merck
Topics to be discussed

- Familial hypercholesterolemia
- LDL apheresis
- Efficacy of PCSK9 monoclonal antibodies
- Trials of PCSK9 antibodies and apheresis
- Comparison of apheresis and PCSK9 monoclonal antibodies
Familial Hypercholesterolemia

- Autosomal co-dominant high LDL
- Heterozygotes: untreated LDL-C 155 - 500 mg/dL
  - Premature CAD
- Homozygotes often have untreated LDL-C >500 mg/dL
  - CAD typically onset in childhood and adolescence
  - Insufficient response to usual lipid lowering medication, even in combination
- High LDL levels, often tendon xanthomases

Nordestgaard B G et al. Eur Heart J 2013;eurheartj.eht273
Treatment of FH

- **Lifestyle changes**
  - Decrease saturated fatty acids to ≤7% of total energy intake; limit dietary cholesterol <200 mg/day; add plant stanol/sterols (2 g daily); soluble fiber (10-20 g daily)
  - Physical activity and weight control
  - **Smoking cessation**

- **Medications**: Statins are best (rosuvastatin, atorvastatin)
- If LDL is not low enough add additional medications (ezetimibe, then colesevelam, niacin)
- LDL apheresis: heterozygotes every 2 weeks, homozygotes weekly
- Homozygous patients: statins, ezetimibe, resins, niacin apheresis, lomitapide, mipomersen
Lipid Lowering Therapies and LDL receptor function

Statins
  Inhibit HMG-CoA reductase, rate limiting step in cholesterol synthesis

Ezetimibe
  Inhibits the absorption of cholesterol

Bile Acid Sequestrants
  Inhibit enterohepatic reuptake of bile acids and increase fecal loss of bile salts

PCSK9 inhibitors
  Inhibit degradation of LDL receptors and increase recycling

All work by increasing expression of LDL receptors

Niacin, lomitapide, mipomersen do not work by upregulating LDL receptors (possibly some effect of high dose statins)
Typical percent LDL-C reduction by statin and dose

<table>
<thead>
<tr>
<th>Treatment (drug/dose)</th>
<th>5 mg</th>
<th>10 mg</th>
<th>20 mg</th>
<th>40 mg</th>
<th>80 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosuvastatin</td>
<td>-40</td>
<td>-46</td>
<td>-52</td>
<td>-55</td>
<td>------</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>------</td>
<td>-37</td>
<td>-43</td>
<td>-48</td>
<td>-51</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>-26</td>
<td>-30</td>
<td>-38</td>
<td>-41</td>
<td>-47*</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>------</td>
<td>-21</td>
<td>-27</td>
<td>-31</td>
<td>-40</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>------</td>
<td>-20</td>
<td>-24</td>
<td>-30</td>
<td>-36</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>------</td>
<td>------</td>
<td>-22</td>
<td>-25</td>
<td>-35</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>------</td>
<td>(1 mg) -32</td>
<td>(2 mg) -36</td>
<td>(4 mg) -43</td>
<td></td>
</tr>
</tbody>
</table>

*Simvastatin 80 mg only in patients already taking for > 1 year and no other contraindications (higher risk of rhabdomyolysis)

Compiled from various clinical trials and package inserts
Estimates of cumulative CHD-free survival in people with FH according to statin treatment (P < 0.001 for difference).

Nordestgaard B G et al. Eur Heart J 2013;eurheartj.eht273
Homozygous FH

- Therapy begins at diagnosis regardless of age
- Statins, ezetimibe and other agents may help but LDL apheresis often necessary
- Cardiovascular disease monitoring critical
- Additional drugs approved for homozygous FH patients over age 18:
  - Mipomersen
  - Lomitapide
Algorithm for management of HoFH

Homozygous Familial Hypercholesterolaemia

LDL-C targets:
- <2.5 mmol/L [<100 mg/dL] (adults)
- <3.5 mmol/L [<135 mg/dL] (children)
- <1.8 mmol/L [<70 mg/dL] if clinical CVD

At diagnosis
Lifestyle and Diet +
Statin
(most efficacious at
highest dose depending on
tolerability)

Ezetimibe 10 mg +
resins or other
drugs*
*Fibrate, nicotinic acid,
probucol (use of these
additional treatments may
be limited by tolerability
and drug availability)

New Therapeutic
options

Future Therapeutic
options

PCSK9
inhibitors

CETP inhibitors

Gene therapy

LDL-Apheresis
As early as possible if available (by 5 years, no later than 8 years)
every 1 or 2 weeks

In selected patients
Liver Transplant

Lomitapide
Approved by FDA, EMA

Mipomersen
Approved by FDA

Risk of first MACE among Homozygous FH patients before and after the introduction of modern lipid lowering therapy.

Benefit from modern lipid therapy (Endpoint: MACE)

LDL Apheresis

- LDL apheresis is a FDA-approved process of selectively removing Apo B-containing particles from the circulation through extracorporeal precipitation with either dextran sulphate cellulose or heparin.
- The procedure must be repeated every 1 to 2 weeks.
- In a single procedure, LDL apheresis typically removes at least 60% of the Apo B-containing lipoproteins.
**LDL-apheresis**

- LDL-apheresis: inadequate response to maximally tolerated therapy in patients with familial hypercholesterolemia
- Requires good vascular access (2 vein sites or A-V fistula)
- Usually done weekly for homozygous patients and every two weeks for heterozygous patients
- Over time 50% reduction of LDL-C
Lipoprotein-apheresis

Pre-Apheresis

• Total Cholesterol 611 mg/dL
• LDL-C 507 mg/dL
• Fibrinogen 446 mg/dL
• CRP 2.0 mg/dL

Post-Apheresis

• Total Cholesterol 216 mg/dL
• LDL-C 134 mg/dL
• Fibrinogen 193 mg/dL
• CRP 0.5 mg/dL

Slide courtesy Dr. Patrick Moriarty
Mean Percentage Reduction of Plasma Proteins with Different Methods of Lipoprotein-apheresis

<table>
<thead>
<tr>
<th>mg/dL</th>
<th>MDF</th>
<th>Lipid Filtration</th>
<th>HELP</th>
<th>DALI</th>
<th>DSA</th>
<th>IA</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>56-62%</td>
<td>61%</td>
<td>55-61%</td>
<td>53-76%</td>
<td>49-75%</td>
<td>62-69%</td>
</tr>
<tr>
<td>HDL-C</td>
<td>25-42%</td>
<td>6%</td>
<td>5-17%</td>
<td>5-29%</td>
<td>4-17%</td>
<td>9-27%</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>53-59%</td>
<td>61%</td>
<td>55-68%</td>
<td>28-74%</td>
<td>19-70%</td>
<td>51-71%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>37-49%</td>
<td>56%</td>
<td>20-53%</td>
<td>29-40%</td>
<td>26-60%</td>
<td>34-49%</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>52-59%</td>
<td>42%</td>
<td>51-58%</td>
<td>13-16%</td>
<td>17-40%</td>
<td>15-21%</td>
</tr>
</tbody>
</table>

High variation of values are partially due to differences in treated plasma and blood volumes. **MDF**, membrane differential filtration; **HELP**, heparin-induced extracorporeal LDL precipitation; **DALI**, direct adsorption of lipoproteins; **DSA**, dextrum sulfate adsorption; **IA**, immunoadsorption.

Moriarty PM. Clinical Lipidology, Ballantyne: A Companion to Braunwald’s Heart Disease; 363-74. 2009
LDL-apheresis (current rules)

- LDL-apheresis: inadequate response to maximally tolerated therapy in patients with familial hypercholesterolemia
  - Functional homozygotes with LDL-C > 500 mg/dl
  - Functional heterozygotes with LDL-C > 300 mg/dl and no evidence of vascular disease
  - Functional heterozygotes with LDL-C > 200 mg/dl and evidence of vascular disease
Candidates for LDL Apheresis: NLA FH recommendations

In patients who, after six months, do not have an adequate response to maximum tolerated drug therapy, LDL apheresis is indicated according to these guidelines:

- **Functional homozygous FH** patients with LDL-C ≥300 mg/dL (or non-HDL-C ≥330 mg/dL).

- **Functional heterozygous FH** patients with LDL-C ≥300 mg/dL (or non-HDL-C ≥330 mg/dL) and 0-1 risk factors.

- **Functional heterozygous FH** patients with LDL-C ≥200 mg/dL (or non-HDL-C ≥230 mg/dL) and high risk characteristics such as ≥2 risk factors or high lipoprotein (a) ≥50 mg/dL using an isoform insensitive assay.

- **Functional heterozygous FH** patients with LDL-C ≥160 mg/dL (or non-HDL-C ≥190 mg/dL) and very high risk characteristics (established CHD, other cardiovascular disease, or diabetes).

LDL Apheresis

- Currently, there are more than 400 patients in North America receiving LDL apheresis therapy at more than 40 centers.

- There is a significant gap between the number of patients receiving LDL apheresis therapy and the number that, according to FDA guidelines, may qualify for LDL apheresis.

Lipoprotein-Apheresis (LA) and the reduction of CV Events

## LA Therapy for Elevated Lp(a) Levels

<table>
<thead>
<tr>
<th>Apheresis</th>
<th>Jaeger</th>
<th>Rosada</th>
<th>Leebmann</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-</td>
<td>Post-</td>
<td>Pre-</td>
</tr>
<tr>
<td></td>
<td>(%) reduction</td>
<td>(%) reduction</td>
<td>(%) reduction</td>
</tr>
<tr>
<td>Patients</td>
<td>120</td>
<td>120</td>
<td>37</td>
</tr>
<tr>
<td>Duration</td>
<td>5.5</td>
<td>5.0</td>
<td>5.2</td>
</tr>
<tr>
<td>LDL-C</td>
<td>125</td>
<td>45</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>(-65%)</td>
<td>(-60%)</td>
<td>(-60%)</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>118</td>
<td>33</td>
<td>112</td>
</tr>
<tr>
<td></td>
<td>(-72%)</td>
<td>(-68%)</td>
<td>(-70%)</td>
</tr>
<tr>
<td>MACE* (total)</td>
<td>297</td>
<td>57</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>(-81%)</td>
<td>(-70%)</td>
<td>(-78%)</td>
</tr>
<tr>
<td>MACE* (per year)</td>
<td>1.05</td>
<td>0.14</td>
<td>2.80</td>
</tr>
<tr>
<td></td>
<td>(-86%)</td>
<td>(-97%)</td>
<td>(-78%)</td>
</tr>
</tbody>
</table>

* MACE = Major Coronary Event

percentages are mean percent change

World-Wide Distribution of Lipoprotein-apheresis Therapy for FH Patients

Fewer than 3,500 FH patients, from a potential world population of 12-30 million, receive regular weekly/biweekly treatments

Slide courtesy Dr. Patrick Moriarty
Proprotein convertase subtilisin/kexin type 9

- Member of the family of proteases involved in degradation of LDL-C receptor
- Mutations leading to loss of function are associated with lifelong low LDL-C levels and decreased risk of cardiovascular disease
- Gain of function mutations lead to increased LDL-C levels
- Loss of function mutations lead to low LDL-C

Mean percentage change in calculated LDL-C from baseline to weeks 2, 4, 6, 8, 10, 12, 16 and 20 in the modified intent-to-treat (mITT) population, by treatment group. All patients receiving stable statin therapy.

Stein et al Lancet 2012; 380: 29-36
Percent LDL-C Change from Baseline to Week 12 with Alirocumab in non-FH Hypercholesterolemic Patients

Mean % change in LDL-C from baseline to weeks 2, 4, 6, 8, 10, and 12 by Q4W treatment group.

McKenney et al. J Am Coll Cardiol 2012;59 2344-2353
Efficacy of Alirocumab
Reduction in LDL-C With 150 mg SQ Q2W

-55.7%
-64.7%
-57.0%

Stein et al. NEJM 2012; 366: 1108-1118
Percent Reduction from Baseline in LDL Cholesterol on Evolocumab as Compared with Placebo by Background Lipid-Lowering Therapy.

PCSK9 Inhibition in FH

- Heterozygous FH
  - Dose dependent LDL-C reductions about 40 to 70% on top of background therapies

- Homozygous FH
  - Receptor defective patients: LDL-C reduction 23%
  - Receptor negative patients: no effect

Effects on patients with heterozygous FH

- **Patient Profile (n=77)**
  - >70% on max dose statin
  - >70% on ezetimibe
  - Baseline LDL-C about 155 mg/dL

- **Treatment results**
  - On-treatment LDL-C about 50 mg/dL
  - LDL-C < 100 = 97%
  - LDL-C < 70 = 81%

Stein et al Lancet 2012; 380: 29-36
Alirocumab and heterozygous FH
### Homozygous FH Patients

Mean % in LDL-C from Baseline to Week 12 With Evolocumab

<table>
<thead>
<tr>
<th>Patients</th>
<th>% Δ LDL-C Evolocumab 420 mg Q2W</th>
<th>% Δ LDL-C Evolocumab 420 mg Q4W</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects (n=8)</td>
<td>-16.5%</td>
<td>-13.9%</td>
</tr>
<tr>
<td>Receptor defective (n=6)</td>
<td>-22.9%</td>
<td>-23.6%</td>
</tr>
<tr>
<td>Receptor negative (n=2)</td>
<td>2.6%</td>
<td>15.3%</td>
</tr>
</tbody>
</table>

Patients
Mean age 34
On intensive statin + ezetimibe Rx
Mean Baseline LDL-C = 442 mg/dL (218-563)

Stein et al. Circulation 2013; 128: 21123-2120
Studies with PCSK9 monoclonal antibodies

- LDL cholesterol lowered as much as 70%
- Decreases of non-HDL cholesterol—60%, triglycerides and lipoprotein (a)—25%
- Effects continue over time—52 week data have been presented
- Side effects infrequent and not much difference between placebo and treatment groups
  - Injection site reactions occasionally
Potential uses for PCSK9 Monoclonal Antibodies

- Familial hypercholesterolemia
  - Some effect in homozygous FH patients who are not receptor negative
  - Significant benefits in patients with heterozygous FH—on top of statins and other medications get LDL-C below 100 mg/dL
- Statin tolerance problems
- High risk patients—pre-existing vascular disease
Alirocumab

- FDA approval July 27, 2015
- Indications: adjunct to diet and:
  - maximally tolerated statin therapy for adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease who require additional lowering of LDL – C
- Dosage: 75 mg or 150 mg sc every two weeks
- Availability: 75 mg or 150 mg pre-filled syringe or injector pens
Evolocumab

- European approval
- FDA approval August 27, 2015
- Indications: adjunct to diet and:
  - maximally tolerated statin therapy for adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease who require additional lowering of LDL – C
  - Other LDL lowering therapies in patients with homozygous familial hypercholesterolemia who require additional LDL- C lowering
Evolocumab

- **Dosage**
  - Heterozygous FH: 140 mg sc every two weeks or 420 mg sc once per month
  - Homozygous FH: 420 mg sc once per month
- 140 mg pre-filled syringes or autoinjector
- 420 mg given as three 140 mg injections
Concerns with PCSK9 monoclonal antibodies

- LDL too low?
  - No increase in side effects seen in subjects with LDL-C <25 mg/dL

- Muscle, cognitive, fertility
  - No problems in the rare double loss-of-function patients
  - No significant increased muscle problems in clinical trials

- Antibodies to PCSK9—rare in the clinical trials

- Will this kind of LDL-C reduction with this treatment improve cardiovascular event rates?
  - Outcomes trials in progress
  - 52 week data suggest decrease CVD events (but very small numbers and post-hoc analysis)

- Cost
ODYSSEY Outcomes

> 40 years old
Hospitalization with ACS in the past 4 months

FOURIER

40 to 85 years old
CV disease at high risk for a recurrent event
Fasting LDL-C ≥ 70 mg/dL
  or non-HDL-C ≥ 100 mg/dL

SPIRE

SPIRE 1 On background lipid lowering treatment.
High risk of a CV event.
Must have an LDL-C >70 to 100 mg/dL or non-HDL-C 100 to 130 mg/dL

SPIRE-2 LDL-C =100 (2.6 mmol)

Alirocumab SQ vs placebo
Up to 64 months
Estimated completion: March 2018

Evolocumab SC vs placebo
60 months
Estimated completion: February 2018

Bococizumab SQ vs placebo
60 months
Estimated completion 2017

Endpoint:
First occurrence of:
CHD death, any non-fatal MI, fatal and non-fatal ischemic stroke, UA requiring hospitalization

Endpoint:
Time to CV death, MI, hospitalization for UA, stroke, or coronary revascularization

Endpoint:
Time to CV death, MI, hospitalization for UA, stroke, or coronary revascularization

www.clinicaltrials.gov
Alirocumab and apheresis

- Study of Alirocumab (REGN727/SAR236553) in Patients With Heterozygous Familial Hypercholesterolemia (HeFH) Undergoing Low-density Lipoprotein (LDL) Apheresis Therapy (ODYSSEY ESCAPE)
- Randomized, double-blind, placebo-controlled, parallel-group study to evaluate the effect of alirocumab in comparison with placebo on the frequency of LDL apheresis treatments in patients with HeFH undergoing LDL apheresis therapy.
- Rate of apheresis treatments during a 12-week period normalized by the number of planned apheresis treatments according to each patient's established schedule at screening

www.clinicaltrials.gov
Alirocumab and apheresis

- Enrollment: 62
- Study Start Date: March 2015
- Estimated Study Completion Date: May 2017
- Inclusion Criteria:
  - Men and women ≥18 years of age at the time of the screening visit
  - Diagnosis of heterozygous familial hypercholesterolemia
  - Currently undergoing LDL apheresis therapy weekly or every 2 weeks for at least 8 weeks prior to the screening visit

www.clinicaltrials.gov
Alirocumab and apheresis

Main exclusion criteria:

- Homozygous FH (familial hypercholesterolemia)
- Background medical lipid-modifying therapy not stable for at least 8 weeks prior to screening visit
- LDL apheresis schedule/apheresis settings not been stable
- LDL apheresis schedule other than QW to Q2W
- New exercise program or exercise or diet not stable
- Presence of clinically significant uncontrolled endocrine disease known to influence serum lipids or lipoproteins
- Known positive test for human immunodeficiency virus
- Patients treated with at least 1 dose of alirocumab or any other anti-PCSK9 monoclonal antibody in any other clinical studies
- Pregnant or breastfeeding women

www.clinicaltrials.gov
Alirocumab and apheresis

- Primary outcome measure:
  - Rate of apheresis treatments during a 12-week period normalized by the number of planned apheresis treatments according to each patient's established schedule at screening

www.clinicaltrials.gov
Evolocumab and apheresis

- Trial Assessing Evolocumab (AMG145) Compared to LDL-C Apheresis in Subjects Receiving LDL-C Apheresis Prior to Study Enrollment
- Randomized, Actively Controlled, Open-label, Multicenter Study of Efficacy and Safety of Evolocumab Compared With LDL Apheresis, Followed by Single-Arm Evolocumab Administration in Subjects Receiving LDL Apheresis Prior to Study Enrollment
- **Purpose**: To evaluate the efficacy of subcutaneous (SC) evolocumab, compared to regularly scheduled low density lipoprotein cholesterol (LDL-C) apheresis, on reducing the need for future apheresis

www.clinicaltrials.gov
Evolocumab and apheresis

Inclusion Criteria:

- Male or female, ≥ 18 years of age
- Receiving regular apheresis for LDL-C lowering at least 3 months immediately prior to lipid screening; treatment goal of LDL-C < 100 mg/dL (2.6 mmol/L); receiving LDL-C apheresis during the last ≥ 4 weeks prior to lipid screening at regular QW or Q2W schedule and with no changes in apheresis type
- On lipid-lowering pharmacological therapy including high-intensity statin dose (moderate-intensity statin dose with attestation that higher dose not appropriate) unless history of statin intolerance
- Lipid-lowering therapy status (ie, any therapy for lowering lipids, including apheresis type and frequency) unchanged for ≥ 4 weeks prior to LDL-C screening
- Pre-apheresis LDL-C ≥ 100 mg/dL and ≤ 190 mg/dL at screening
- Fasting triglycerides ≤ 400 mg/dL at screening.

www.clinicaltrials.gov
Evolocumab and apheresis

Exclusion criteria:

- Known homozygous familial hypercholesterolemia
- Missing any apheresis session is medically contraindicated or inappropriate
- Stopping apheresis would be inappropriate in the opinion of the investigator even if LDL-C is controlled to < 100 mg/dL with other therapies
- Myocardial infarction, unstable angina, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) or stroke within 3 months prior to randomization.
- Uncontrolled hypertension

www.clinicaltrials.gov
Evolocumab and apheresis

- Evolocumab or Low Density Lipoprotein Cholesterol (LDL-C) Apheresis
  - Subjects will receive evolocumab q 2 weeks
  - Subjects will continue apheresis at the same schedule, every week (QW) or every two weeks (Q2W), as prior to study entry, for the first 6 weeks

- Endpoints
  - Apheresis avoidance at the end of randomized therapy, defined as no apheresis at week 5 and week 6

www.clinicaltrials.gov
Evolocumab and apheresis

- Estimated Enrollment: 50
- Study Start Date: December 2015
- Estimated Study Completion Date: March 2017
- Estimated Primary Completion Date: January 2017 (Final data collection date for primary outcome measure)
PCSK9 Mab: Possible effects on apheresis

- Some patients are able to discontinue apheresis
- Decrease apheresis to once per month
- Insufficient effect
- Severe vascular disease with elevated LDL cholesterol and lipoprotein (a)—may be helped by use of both modalities
- Elevated lipoprotein (a)—some effect of PCSK9 Mab but more direct removal by apheresis
Effects on apheresis centers

- Small pheresis center
- Four patients—3 HeFH, 1 HoFH
  - One patient on PCSK9 Mab prescribed by her cardiologist--has discontinued apheresis
  - One patient on alirocumab 150 mg q 2 weeks, pheresis currently once every 4 weeks
  - One patient just starting PCSK9 and continuing pheresis every two weeks: some improvement pre pheresis LDL-C
  - Double heterozygous patient on q 2 week pheresis
Advantages of PCSK9

- Levels stable over time instead of going up between treatment sessions (especially every 2 week pheresis)
- Benefit in terms of time and travel (many patients do not have apheresis available)
- No need for venous access
- Costs less than apheresis
Advantages of LDL apheresis

- Fibrinogen decreases
- Better effect in receptor null homozygous patients and some severe heterozygous patients
- Feasible during pregnancy
- Use in pediatric patients
Cost considerations

- Pheresis about $2500 to 3000 per session – about $65,000 to 70,000 per year if every two weeks (does not necessarily include lab work, transportation costs, vascular access costs)
- Alirocumab and evolocumab about $14,000 per year
- Combination PCSK9 plus monthly apheresis would be about $50,000 per year
- Cost benefit analysis of PCSK9 will depend on outcomes trial data as well as eventual cost of the medication
Conclusions

- PCSK9 monoclonal antibodies reduce atherogenic lipoproteins
- They work in patients with heterozygous FH and some effect in homozygous FH
- Safety data look good to date
- Alirocumab and evolocumab now approved
- Long term outcome studies are in progress
- Potential to decrease frequency of or discontinue apheresis in many patients
- Likely significant benefit to patients who do not have access to apheresis