Breaking Bad Cholesterol: The Latest Dyslipidemia Management Strategies

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Walter P. Scheffe 2023 CPE Series
October 28, 2023

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Financial Disclosure and Resolution

Under guidelines established under the Standards for Integrity and Independence in Accredited Continuing Education, disclosure must be made regarding relevant financial relationships with ineligible companies within the last 24 months.

Jordan Fuller

I have no relevant financial relationship with ineligible companies to disclose.

2

Professional Practice Gap

- Since the publication of the 2018 guidelines for the management of blood cholesterol, a number of new recommendations and medications have come to market that may change current management of dyslipidemia.
- This presentation will review old guidelines and discuss current therapy recommendations as well as review new medications that have come to market in recent years for the management of dyslipidemia.

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Learning Objectives

At the completion of this activity, pharmacists will be able to:

1. Interpret treatment recommendations included in the 2018 ACC-AHA, 2019 ESC/EAS, and 2020 AACE/ACE hypercholesterolemia guidelines
2. Explain the role of nonstatin therapies for LDL-cholesterol management
3. Apply guidelines for the management of patients with hypercholesterolemia

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Outline

2018 ACC/AHA Guideline Review and Referenced Non-Statins:
- Ezetimibe
- PCSK-9 Inhibitors

Recent Guideline Updates and Referenced Non-Statins:
- Icosapent ethyl
- Bempidoic Acid
- Inclisiran

Future Agents
- Evinacumab-dgnb
- Lomitapide

Summary and Application

5

Patient Case

AG is a 67-year-old Hispanic male with a past medical history of hypertension, gout, peripheral artery disease and myocardial infarction (6 months ago) being seen in clinic today for a follow-up visit.

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HDL-C = 42 mg/dL
Non-HDL-C = 121 mg/dL
TG = 140 mg/dL
LDL-C = 93 mg/dL

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- > 30% LDL-C reduction; LDL-C < 70 mg/dL
- > 50% LDL-C reduction; LDL-C < 70 mg/dL
- > 50% LDL-C reduction; LDL-C < 55 mg/dL

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Recent Guidelines

2018

- AHA/ACC Multisociety Guideline on the Management of Blood Cholesterol

2019

- ESC/EAS Guidelines for the management of dyslipidemias

2020

- AACE/ACE guidelines for the management of dyslipidemia and prevention of cardiovascular disease

2021

- ACC Expert Consensus Decision Pathway (ECDP) on the Management of ASCVD Risk Reduction in Patients with Persistent Hypertriglyceridemia

2022

- USPSTF: Recommendations on Statin Use for the Primary Prevention of Cardiovascular Disease in Adults
- ACC ECDP on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

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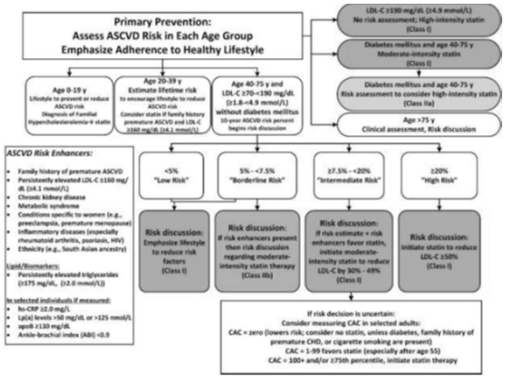
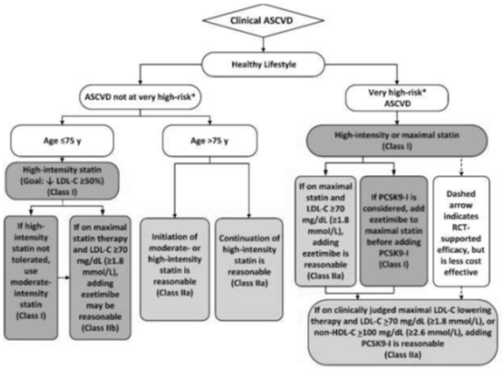
Primary vs. Secondary Prevention





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"Statin" Benefit Groups

Severe hypercholesterolemia (LDL ≥ 190)	Age 40-75 years, with diabetes, and LDL ≥ 70 mg/dL
Age 40-75 years, without diabetes, LDL ≥ 70, and 10-yr ASCVD risk ≥ 7.5%	Clinical ASCVD

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LDL-C Goal

LDL-C ≤ 100 mg/dL
- Primary severe hypercholesterolemia

LDL-C ≤ 70 mg/dL
- Very high risk ASCVD

50% reduction in LDL-C
- Age 40 – 75 years, with diabetes and risk factors, and LDL-C ≥ 70 mg/dL
- Age 40 – 75 years, without diabetes, LDL-C ≥ 70 mg/dL, and ASCVD risk ≥ 20%

30% reduction in LDL-C
- Age 40 – 75 years, without diabetes, LDL-C ≥ 70 mg/dL, and ASCVD risk 7.5 – 19.9%

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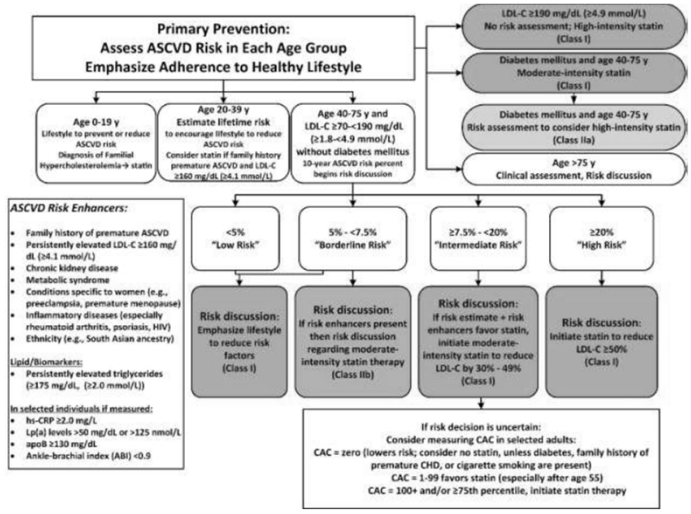
Primary Prevention



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Risk Enhancing Factors

Family history of premature ASCVD

High risk ethnicities

Persistently elevated LDL-C ≥ 160 mg/dl

Persistently elevated, primary hypertriglyceridemia (≥ 175 mg/dl)

Metabolic syndrome

Inflammatory disease
- HIV
- Psoriasis
- Rheumatoid arthritis

Conditions specific to women
- Pre-eclampsia
- Premature menopause (< 40 yo)

High sensitivity (hs)-C reactive protein (CRP) > 2.0 mg/L

Ankle-brachial index (ABI) < 0.9

Chronic kidney disease (CKD)

Elevated lipoprotein (a)

Elevated apoB

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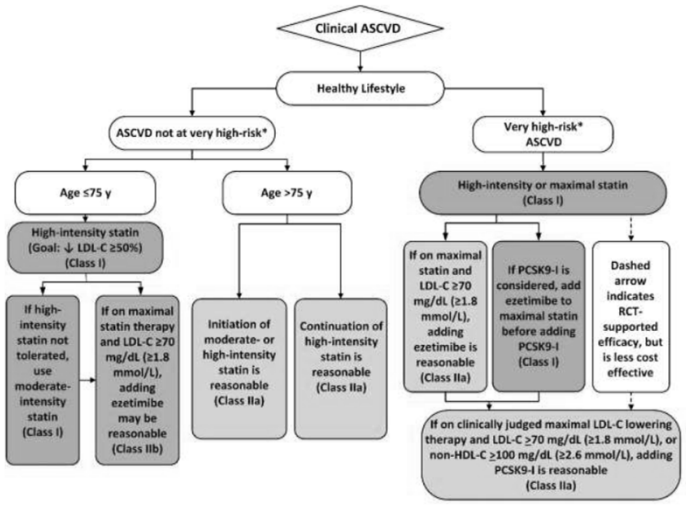
Secondary Prevention



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What constitutes very high-risk?

Major ASCVD events
• Recent ACS (within past 12 months) • History of MI • History of ischemic stroke • Symptomatic PAD

High-risk conditions
• Age ≥ 65 years • Heterozygous familial hypercholesterolemia • History of prior CABG or PCI outside of major ASCVD events • Diabetes • Hypertension • Chronic kidney disease (eGFR 15-59 ml/min/1.73m^2 • Persistently elevated LDL (≥ 100) despite maximally tolerated statin therapy and ezetimibe • History of heart failure

History of multiple major ASCVD events

or

1 major ASCVD event and multiple high-risk conditions

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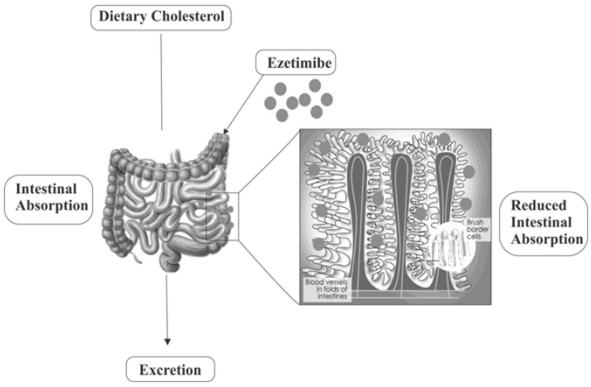
Ezetimibe

MOA

- Inhibit the action of the transporter NPC1L1
  - Blocks cholesterol absorption across intestinal border
  - Reduces the delivery of chylomicron cholesterol to the hepatocyte via the portal circulation

Drugs and dosing

- Ezetimibe (Zetia) 10 mg daily
- Typically used in combination with statin (Vytorin – simvastatin/ezetimibe)



https://drugsdetails.com/ezetimibe/

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Ezetimibe

Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes		
Study Design	Multi-center, double-blind, randomized controlled trial	
Population	Patients ≥ 50 yo hospitalized for ACS within the preceding 10 days with: • LDL-C levels 50 – 100 mg/dL if receiving lipid lowering therapy • LDL-C levels 50 – 125 mg/dL if not receiving lipid lowering therapy	
Intervention	Simvastatin (40mg/d) + ezetimibe (10mg/d)	Placebo + simvastatin (40mg/day)
Endpoints	Composite of cardiovascular death, nonfatal myocardial infarction, unstable angina requiring rehospitalization, coronary revascularization (> 30 days after randomization), or nonfatal stroke	
Conclusion	CV mortality, major CV event, or nonfatal stroke • 34.7% vs. 32.7% (HR 0.94; 95% CI 0.89-0.99; P=0.016; NNT 50)	

Among individuals with recent ACS, the addition of ezetimibe to moderate-intensity statin therapy is associated with a reduction in CV mortality, major CV event, or nonfatal stroke when compared to statin therapy alone

NEJM. 2015. 375(25):2387-2397

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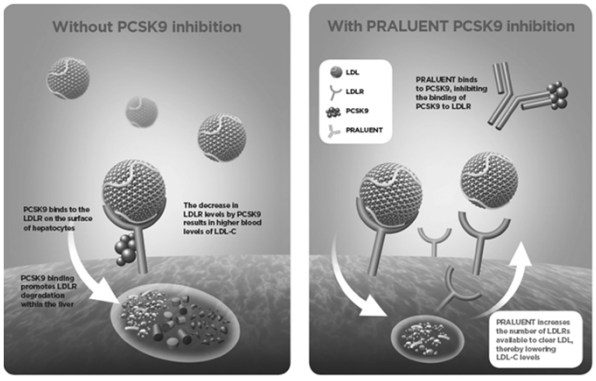
PCSK9 Inhibitors

MOA

- Human monoclonal antibody to PCSK9 (proprotein convertase subtilisin kexin type 9, a protein that degrades the LDL receptor)
- Binds to PCSK9 and increases the number of LDL receptors available to clear circulating LDL.

Drugs and dosage

- Alirocumab (Praluent) 75 or 150 mg SQ every 2 weeks
- Evolocumab (Repatha) 140 mg SQ every 2 weeks or 420 mg SQ once a month



https://european-biotechnology.com/up-to-date/latest-news/news/sanofis-alirocumab-improves-cardiovascular-event-rate-over-statins.html

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PCSK9 Inhibitors

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease		
Study Design	Multi-center, double-blind, randomized placebo controlled trial	
Population	Patients > 40 yo and < 85 yo with clinical ASCVD and risk factors • LDL-C levels ≥ 70 mg/dL receiving background statin therapy	
Intervention	Evolocumab 140 mg SQ Q2W or Evolocumab 420 mg SQ monthly	Matching placebo
Endpoints	Composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization	
Conclusion	CV mortality, major CV event, or nonfatal stroke • 9.8% vs. 11.3% [HR 0.85, 95% CI 0.79-0.92, p<0.001]	

Among patients with clinical atherosclerotic disease and LDL > 70 despite high- or moderate-intensity statin therapy, the addition of evolocumab resulted in a reduction in major cardiovascular events at median follow-up 26 months.

NEJM. 2017. epub 2017-03-17:1-10

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PCSK9 Inhibitors

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome		
Study Design	Multi-center, double-blind, randomized placebo controlled trial	
Population	Patients ≥ 40 yo with history of ACS in the previous 1 – 12 months • LDL-C levels ≥ 70 mg/dL receiving maximally tolerated statin therapy	
Intervention	Alirocumab 75 mg SQ Q2W (titrated up to 150 mg to maintain target LDL-C)	Matching placebo
Endpoints	Composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization	
Conclusion	CV mortality, major CV event, or nonfatal stroke • 9.5% vs. 11.1% [HR 0.85, 95% CI 0.73-0.98, p<0.001]	

Among individuals with previous ACS receiving maximally tolerated statin therapy, the addition of alirocumab is associated with a reduction in risk of recurrent ischemic cardiovascular events.

N Engl J Med 2018; 379:2097-2107

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Recent Guideline Updates

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According to more recent guidelines, what is the target LDL-C reduction and LDL-C threshold for this patient?

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According to more recent guidelines, which change in lipid lowering regimen is recommended?

- Continue current regimen unchanged
- Add ezetimibe
- Add alirocumab
- Add icosapent ethyl

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2018
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FYI

2019 ESC/ESA Guidelines

Treatment Goals for LDL-C:
- High risk: Reduction of > 50% from baseline and goal < 70 mg/dL
- Very-high risk: Reduction of > 50% from baseline and goal < 55 mg/dL
  - ASCVD
  - Diabetes w/ target organ damage, >3 major risk factors, or early onset Type 1 (>20 years)
  - Severe CKD (eGFR <30 mL/min/1.73 m2)
  - A calculated SCORE > 10% for 10-year risk of fatal CVD
  - FH with ASCVD or with another major risk factor

Pharmacological LDL-C lowering:
- If goals not achieved with maximum tolerated statin, combination with ezetimibe is recommended
- If goals not achieved with maximum tolerated statin and ezetimibe for secondary prevention, a combination with a PCSK9 inhibitor is recommended

Mach F et al. Eur Heart J. 2020;41(1):111-88

FYI

2020 AACE/ACE

	Low-Risk	High to Moderate Risk	Very High Risk	Extreme Risk
LDL	< 130 mg/dL	< 100 mg/dL	< 70 mg/dL	< 55 mg/dL
Non-HDL	< 160 mg/dL	< 130 mg/dL	< 100 mg/dL	< 80 mg/dL
ApoB	NR	< 90 mg/dL	< 80 mg/dL	< 70 mg/dL
TG	< 150 mg/dL for all risk categories			

Continued emphasis on lifestyle recommendations

Support measuring Lp(a) in higher-risk individuals

Use of icosapent ethyl to prevent ASCVD

Handelsman Y et al. Endocr Pract. 2020;26(10):1196-1224

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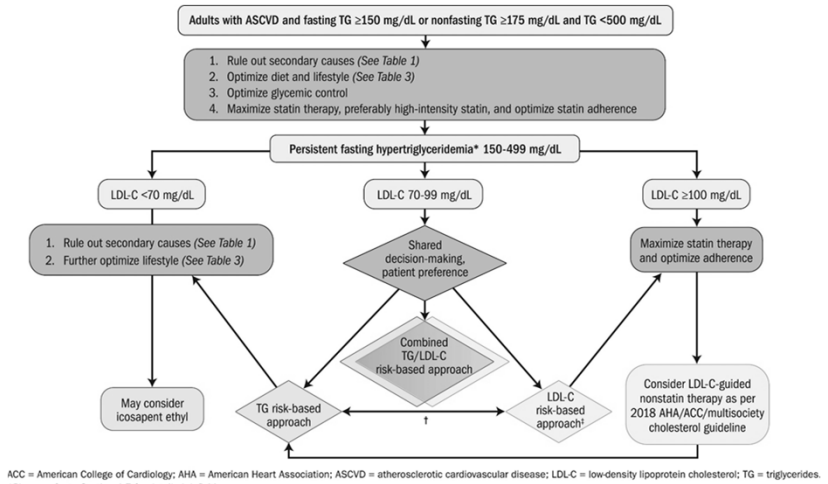
FYI

2021 ACC Consensus Pathway



ACC = American College of Cardiology; AHA = American Heart Association; ASCVD = atherosclerotic cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; TG = triglycerides.
*Please refer to Section 4.7 for detailed definition.
†Clinicians could use a TG risk-based approach once LDL-C levels are optimized and vice versa.
‡Patients at very high risk are most likely to benefit from the addition of LDL-C risk-based nonstatin therapies.

Virani SS et al. J Am Coll Cardiol. 2021;78(9):960-993

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Omega-3 fatty acids

MOA

- Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) compete for the enzymes that cause TG synthesis, but do so poorly resulting in less TG synthesis, enhance TG clearance.
- May have additional benefits in change in immune function and cellular proliferation and antioxidative actions.

Drugs and dosing

- Prescription combination of EPA and DHA: Lovaza
- **Prescription ethyl ester of EPA only: Vascepa**
- OTC dietary supplement: various brands/generics
- Target dosing 2-4 g/day (in 1 or 2 daily doses)

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Omega-3 Fatty Acids

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia		
Study Design	Multi-center, double-blind, randomized placebo controlled trial	
Population	Patients ≥ 45 yo with clinical ASCVD or ≥ 50 yo with diabetes and ≥ 1 risk factor • Fasting TG levels ≥ 150 mg/dL and < 500 mg/dL • LDL-C levels > 40 mg/dL and ≤ 100 mg/dL receiving stable statin therapy	
Intervention	Icosapent Ethyl 2 g PO BID with food	Matching placebo
Endpoints	Composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, hospitalization for unstable angina, or coronary revascularization	
Conclusion	CV mortality, major CV event, or nonfatal stroke • 17.2% vs. 22.0% [HR 0.75, 95% CI 0.68-0.83, p<0.001]	

In patients with established atherosclerotic heart disease, or diabetes and an additional risk factor, on pre-existing statin therapy with residual hypertriglyceridemia, icosapent ethyl was associated with a reduction in cardiovascular events and cardiovascular death.

N Engl J Med 2019; 380:11-22

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2022 ACC Consensus Pathway

Clinical ASCVD at Very-High Risk on Statin for Secondary Prevention

>50% LDL-C reduction and LDL-C <55 mg/DL (or non-HDL-C <85 mg/dL) on maximally-tolerated statin therapy

1. Evaluate and optimize lifestyle modifications, adherence to guideline-recommended statin therapy, risk factor control, and SASEs
2. Increase to high-intensity statin therapy if not already taking

Consider the following as the initial nonstatin agent and addition of other agents as needed to achieve desired reduction of LDL-C

Consider ezetimibe and/or PCSK9 inhibitor

May consider bempedoic acid or inclisirin

Lloyd-Jones, DM et al. J Am Coll Cardiol. 2022;S0735-1097

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2022 ACC Consensus Pathway

Clinical ASCVD NOT at Very-High Risk on Statin for Secondary Prevention

>50% LDL-C reduction and LDL-C <55 mg/DL (or non-HDL-C <85 mg/dL) on maximally-tolerated statin therapy

1. Evaluate and optimize lifestyle modifications, adherence to guideline-recommended statin therapy, risk factor control, and SASEs
2. Increase to high-intensity statin therapy if not already taking

Consider the following as the initial nonstatin agent and addition of other agents as needed to achieve desired reduction of LDL-C

Consider ezetimibe

May consider adding or replacing with PCSK9 inhibitor

May consider bempedoic acid or inclisirin

Lloyd-Jones, DM et al. J Am Coll Cardiol. 2022;S0735-1097

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Bempidoic Acid

MOA
- An adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers LDL-C by inhibition of cholesterol synthesis in the liver

Dose
- Bempidoic Acid 180 mg orally once daily

General Information
- FDA approved February 2020
- Mean LDL-C reduction varies from 15 – 30%
- Effect on cardiovascular disease and mortality have not been determined
  - Currently being studied in the OUTCOMES trial (anticipated publication 2023)

Indication
- Adjust to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous FH or established ASCVD who require additional lowering of LDL-C

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Bempidoic Acid

Trial (year)	Patient Population	Intervention	Baseline LDL-C	Mean Treatment ↓ LDL-C
HARMONY (2019)	2,230 pts w/ ASCVD, HeFH or both receiving max tolerated statin	BDA 180 mg vs. placebo + BT	102-103	16.5%
WISDOM (2019)	779 pts w/ ASCVD, HeFH or both receiving max tolerated statin	BDA 180 mg vs. placebo + BT	120	15.1%
SERENITY (2019)	345 pts w/ history of statin intolerance to > 2 statins	BDA 180 mg vs. placebo + BT	158	21.4%
TRANQUILTY (2018)	269 pts w/ history of statin intolerance w/ no statin or low-dose statin	BDA 180 mg vs. placebo + BT	128	28.4%
OUTCOMES (2023)*	14,014 pts w/ history of CVD or high-risk for CVD w/ reported statin intolerance	BDA 180 mg vs. placebo + BT	139	21.1%

N Engl J Med. 2019 Mar 14;380(11):1022-1032; JAMA. 2019 Nov 12;322(18):1780-1788.; J Am Heart Assoc 2019;8:e011662; Atherosclerosis. 2018 Oct;277:195-203; N Engl J Med. 2023 Apr 13;388(15):1353-1364

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Inclisiran

MOA
- Small interfering RNA (siRNA) that inhibits the hepatic translation proprotein convertase subtilisin-kexin type 9 (PCSK9), thereby upregulating the number of LDL-receptors on the hepatocytes

Dose
- Inclisiran 284 mg subcutaneous injection initially and then again at 3 months and then every 6 months

General Information
- FDA approved December 2021
- Mean LDL-C reduction in initial trials was ~50%
- Effect on cardiovascular disease and mortality have not been determined

Indication
- As adjust to diet and maximally tolerated statin therapy for the treatment of adults with ASCVD or heterozygous FH who require additional lowering of LDL-C

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Inclisiran

Trial (year)	Patient Population	Intervention	Baseline LDL-C	Mean Treatment ↓ LDL-C
ORION-10/11 (2020)	3,178 pts w/ ASCVD or ASCVD Risk Equivalents	Inclisiran vs. placebo	105	51.3% (ORION-10) 45.8% (ORION-11)
ORION-3 (2023)	490 pts w/ ASCVD or ASCVD Risk Equivalents	Inclisiran vs. placebo	130	44.2%
*ORION-4 (TBD)	15000 pts w/ ASCVD	Inclisiran vs. placebo	--	--
ORION-8 (TBD)	3275 pts w/ ASCVD, ASVD Risk Equivalents, HeFH, or HoFH	Inclisiran vs. placebo	--	--

*MACE Outcome

N Engl J Med. 2020 Apr 16;382(16):1507-1519; Lancet Diabetes Endocrinol. 2023 Feb;11(2):109-119

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- Add alirocumab
- Add icosapent ethyl

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Future Agents

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Evinacumab-dgnb

MOA
- Recombinant human monoclonal antibody that binds to and inhibits ANGPTL3
  - ANGPTL3 is a member of the angiopoietin-like protein family that is expressed primarily in the liver and plays a role in the regulation of lipid metabolism by inhibiting lipoprotein lipase (LPL) and endothelial lipase (EL)
  - Inhibition of ANGPTL3 leads to reduction in LDL-C, HDL-C, and triglycerides (TG)

Dose
- Recommended dose is 15 mg/kg administered by intravenous (IV) infusion once monthly

General Information
- FDA approved February 2021

Indication
- As an adjunct to other LDL-C lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with HoFH

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Lomitapide

MOA
- Binds to and inhibits microsomal triglyceride transfer protein (MTP) in the endoplasmic reticulum
  - MTP inhibition prevents the assembly of Apo B containing lipoproteins in enterocytes and hepatocytes resulting in reduced production of chylomicrons and VLDL and subsequently reduced plasma LDL-C

Dose
- Recommended dose is 15 mg/kg administered by intravenous (IV) infusion once monthly

General Information
- FDA approved February 2012 as adjunct to other lifestyle modifications and lipid-lowering agents including lipid apheresis in patients with HoFH

Black Boxed Warning
- Hepatotoxicity (REMS Program Only)

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Summary and Application

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Conclusion and Clinical Pearls

Clinical ASCVD at very high risk and patients with clinical ASCVD and FH on high-intensity statin therapy, a lower LDL-C threshold of LDL-C ≥55 mg/dL (or non–HDL-C ≥85 mg/dL) is recommended for addition of nonstatin therapy.

Clinical ASCVD not at very high-risk, ezetimibe 10 mg daily should be the initial nonstatin agent, given the benefits on ASCVD outcomes with potential second step of PCSK9 inhibitors if needing further LDL-C lowering.

Decisions to add nonstatin therapy should be based on the patient's risk, percent LDL-C reduction with statin therapy and LDL-C thresholds

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What changes do you intend to make in your practice as a result of this activity?

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Additional Resources

Grundy SM et al. J Am Coll Cardiol. 2019; 73(24):e285-e350.

Mach F et al. Eur Heart J. 2020;41(1):111-88

Handelsman Y et al. Endocr Pract. 2020;26(10):1196-1224

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References

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019 Jun 25;73(24):e285-e350. doi: 10.1016/j.jacc.2018.11.003. Epub 2018 Nov 10. Erratum in: J Am Coll Cardiol. 2019 Jun 25;73(24):3237-3241. PMID: 30423393.

Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020 Jan 1;41(1):111-188. doi: 10.1093/eurheartj/ehz455. Erratum in: Eur Heart J. 2020 Nov 21;41(44):4255. PMID: 31504418.

Handelsman Y, Jellinger PS, Guerin CK,et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm - 2020 Executive Summary. Endocr Pract. 2020 Oct;26(10):1196-1224. doi: 10.4158/CS-2020-0490. PMID: 33471721.

Virani SS, Morris PB, Agarwala A, et al. 2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients With Persistent Hypertriglyceridemia: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021 Aug 31;78(9):960-993. doi: 10.1016/j.jacc.2021.06.011. Epub 2021 Jul 28. PMID: 34332805.

Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2022 Oct 4;80(14):1366-1418. doi: 10.1016/j.jacc.2022.07.006. Epub 2022 Aug 25. Erratum in: J Am Coll Cardiol. 2023 Jan 3;81(1):104. PMID: 36031461.

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References

Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. N Engl J Med. 2015 Jun 18;372(25):2387-97. doi: 10.1056/NEJMoa1410489. Epub 2015 Jun 3. PMID: 26039521.

Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. N Engl J Med. 2017 May 4;376(18):1713-1722. doi: 10.1056/NEJMoa1615664. Epub 2017 Mar 17. PMID: 28304224.

Schwartz GG, Steg PG, Szarek M, et al. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. N Engl J Med. 2018 Nov 29;379(22):2097-2107. doi: 10.1056/NEJMoa1801174. Epub 2018 Nov 7. PMID: 30403574.

Ray KK, Bays HE, Catapano AL, et al; CLEAR Harmony Trial. Safety and Efficacy of Bempedoic Acid to Reduce LDL Cholesterol. N Engl J Med. 2019 Mar 14;380(11):1022-1032. doi: 10.1056/NEJMoa1803917. PMID: 30865796.

Goldberg AC, Leiter LA, Stroes ESG, et al. Effect of Bempedoic Acid vs Placebo Added to Maximally Tolerated Statins on Low-Density Lipoprotein Cholesterol in Patients at High Risk for Cardiovascular Disease: The CLEAR Wisdom Randomized Clinical Trial. JAMA. 2019 Nov 12;322(18):1780-1788. doi: 10.1001/jama.2019.16585. Erratum in: JAMA. 2020 Jan 21;323(3):282. PMID: 31714986; PMCID: PMC6865290.

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References

Laufs U, Banach M, Mancini GBJ, et al. Efficacy and safety of bempedoic acid in patients with hypercholesterolemia and statin intolerance. J Am Heart Assoc 2019;8:e011662.

Ballantyne CM, Banach M, Mancini GBJ, et al. Efficacy and safety of bempedoic acid added to ezetimibe in statin-intolerant patients with hypercholesterolemia: A randomized, placebo-controlled study. Atherosclerosis. 2018 Oct;277:195-203. doi: 10.1016/j.atherosclerosis.2018.06.002. Epub 2018 Jun 12. PMID: 29910030.

Nissen SE, Lincoff AM, Brennan D, et al. Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. N Engl J Med. 2023 Apr 13;388(15):1353-1364. doi: 10.1056/NEJMoa2215024. Epub 2023 Mar 4. PMID: 36876740.

Ray KK, Troquay RPT, Visseren FLJ, et al. Long-term efficacy and safety of inclisiran in patients with high cardiovascular risk and elevated LDL cholesterol (ORION-3): results from the 4-year open-label extension of the ORION-1 trial. Lancet Diabetes Endocrinol. 2023 Feb;11(2):109-119. doi: 10.1016/S2213-8587(22)00353-9. Epub 2023 Jan 5. PMID: 36620965

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