Lipid Update and Case Studies: Comparing ATP III, AHA/ACC Guidelines and the National Lipid Association Recommendations 2017

Chad Link, DO FACC
Cardiologist
Chairman Cardiology Section
Sparrow TCI

Disclosures

Speakers Bureau – Actelion Pharmaceuticals, Bristol-Myers Squibb, Pfizer

Clinical Research Support– Sanofi Aventis

Patient Case #1

- 54 year old Hispanic male with type 2 diabetes, hypertension and CAD presents for an initial visit. He quit smoking 2 years ago and follows a low-calorie diet.

- Medications: lisinopril 10 mg daily, atorvastatin 40 mg daily and aspirin 81 mg daily

- Lipid Profile: TC 180 mg/dl, LDL-C 110 mg/dl, HDL-C 40 mg/dl, TG 150 mg/dl, LFTs NL

Patient Case #1

Is this patient to goal? What would be your recommendations? (54 Year Old, DM, CAD)

(TC 180 mg/dl, LDL-C 110 mg/dl, HDL-C 40 mg/dl, TG 150 mg/dl on atorvastatin 20 mg)

A. Continue current therapy. (ACC/AHA Guidelines)
B. Adjust or change statin to a goal LDL of < 70 mg/dl (High risk patient- NLA Guidelines)
C. Add additional lipid agents to regimen.
D. Consider alternative therapy

Patient Case #1

Having determined his therapeutic LDL goal of < 70 mg/dl, how do you treat his hyperlipidemia? (54 Year Old, DM, CAD)

(TC 180 mg/dl, LDL-C 110 mg/dl, HDL-C 40 mg/dl, TG 150 mg/dl on atorvastatin 20 mg)

A. Continue atorvastatin 40 mg daily (ACC/AHA Guidelines)
B. Increase to atorvastatin 80 mg daily (NLA Guidelines)
C. Add ezetimibe 10 mg to atorvastatin 40 mg daily (NLA)
D. Add niacin 1000 mg to atorvastatin 40 mg daily (NLA)
E. Change to rosuvastatin 40 mg daily (NLA)
F. Add alirocumab 75 mg 2x monthly to atorvastatin 40 mg daily

Objectives

- Review Current Guidelines and Recommendations from the ACC/AHA, AACE and the National Lipid Association

- Discuss Emerging Therapies in the Treatment of Hyperlipidemia

- Case Studies

Summary of Recommendations

- ATP III Summary
- 2013 ACC/AHA Guidelines
- National Lipid Association lipid management approaches for ASCVD prevention

National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) Guidelines

- U.S. guidelines for the detection, evaluation, and treatment of hyperlipidemia in adults
- Developed by an expert panel for the National Heart, Lung, and Blood Institute (NHLBI)
  - Division of National Institutes of Health (NIH)
  - Long history of developing clinical practice guidelines
    - First JNC report published 1976
- ATP release history:
  - ATP I First released in 1988
  - ATP II 1993 (LDL goal < 100 mg/dl)
  - ATP III 2001 (LDL goal < 100 mg/dl and FRS)

U.S. Guidelines for Management of Dyslipidemias

2001	NCEP ATP III guidelines (TG < 150, DM CV risk, non HDL)
2004	NCEP ATP III implications (LDL < 70 mg/dl optional)
2008	ADA/ACCF Consensus Statement on Lipoprotein Management in Patients with Cardiometabolic Risk (LDL < 70 mg/dl)
2011	AHA/ACC guidelines for secondary prevention (LDL < 70 mg/dl for high risk patients)
2012	AACE Guidelines for the Management of Dyslipidemia and Prevention of Atherosclerosis
2013	ATP IV Recommendations
2013	National Lipid Association Recommendations

AACE = American Association of Clinical Endocrinologists, ACC = American College of Cardiology, ACCF = American College of Cardiology Foundation, ADA = American Diabetes Association, AHA= American Heart Association

ATP III Classification of Cholesterol Concentrations

Lipoprotein	Concentration (mg/dL)	Interpretation
TC	< 200 200-239 ≥240	Desirable Borderline high High
LDL-c	<100 100-129 130-159 160-189 ≥190	Optimal Near/above optimal Borderline high High Very high
HDL-c	<40 ≥60	Low High
TG	<150 150-199 200-499 ≥500	Normal Borderline high High Very high

ATP III Classification of Cholesterol Concentrations

Risk Category	LDL Goal	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalents (10-year risk >20%)	<100 mg/dL	≥100 mg/dL	≥130 mg/dL (100-129 mg/dL: drug optional)*
2+ Risk Factors (10-year risk ≤20%)	<130 mg/dL	≥130 mg/dL	10-year risk 10-20%: ≥130 mg/dL 10-year risk <10%: ≥160 mg/dL
0-1 Risk Factor†	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

ATP III Treatment Targets

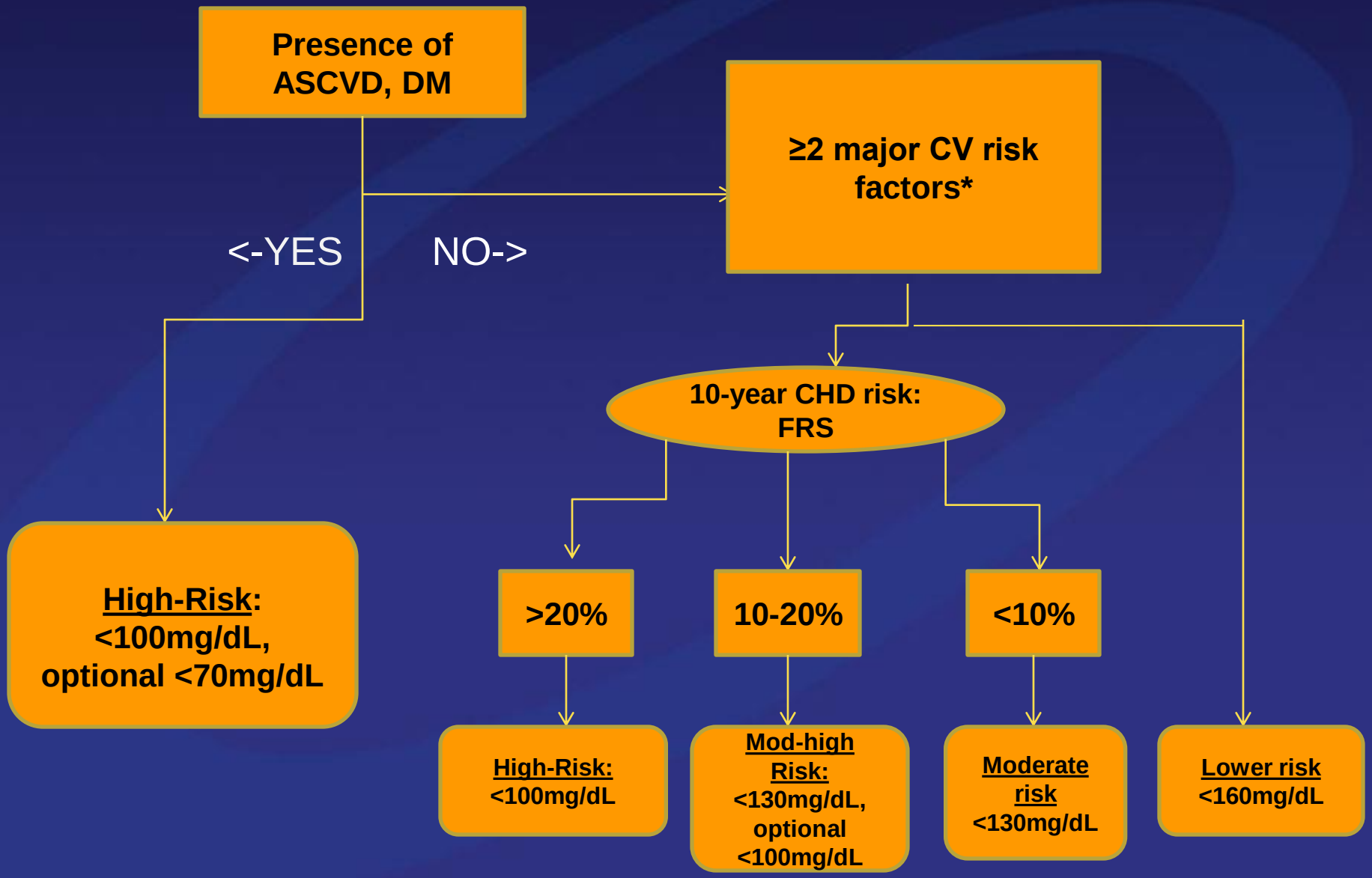
Primary Target:
LDL-c

Secondary Target:
Non-HDL-c

(Once LDL goal met and if TG ≥200)

Exception: TG lowering is an immediate target if ≥ 500 mg/dL

NCEP ATP III: Determining LDL-c Goals



Major Studies Published Since 2001

Statin Trials

- HPS
- PROVE-IT
- ASCOT
- PROSPER
- ALLHAT
- TNT

Non-Statin Trials

- 2 Niacin trials
- 2 Fibrate Trials
- IMPROVE IT
- Fourier

ATP IV Guidelines

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Scope of Guideline

- To identify whom to treat, with what treatment(s), and to consider how intensively the treatments should be used
- The recommendations were designed to be easy to use in the clinical setting
- The report does not provide for a comprehensive approach to the detection, evaluation, and treatment of lipid disorders as was done in the prior ATP III Report

ACC/AHA (With NHLBI) Guidelines: 4 New Guidelines

- Cholesterol Management
- Risk assessment
- Obesity
- Lifestyle recommendations

Atherosclerotic Disease Risk: What's new?

- CVA/ TIA (presumed to be atherosclerotic in origin) risk added to MI (especially important for African Americans and women)
- Newly developed race and sex specific equations
- Considered other markers. Did not add any. "none merited inclusion." Four markers may be considered if uncertainty persists after use of equation.
  - Family History (if known first degree relative male <55 or female <65)
  - Hs-CRP (2 mg/L)
  - CAC- strongest evidence is for this marker (300 Agatston units)
  - ABI (< 0.9)

Four Major Statin Benefit Groups

1. Does the patient have a history of heart disease (ASCVD) or stroke?

2. Is the LDL > 190 mg/dL? Do they have Familial Hyperlipidemia

3. Does the patient have DM, 40-75 years old with an LDL of 70-189 mg/dL without ASCVD?

4. Does the patient without DM or ASCVD have a global risk score > 7.5% for primary prevention of risk assessment?

ACC/AHA Statin Benefit Groups

H=High intensity statin; M=Moderate intensity statin

- Individuals with clinical ASCVD without New York Heart Association class II-IV heart failure or receiving hemodialysis (**H preferred; M if age >75 or if not candidate for H**).
- Individuals with primary elevations of LDL-C ≥190 mg/dl (**H preferred; M if not candidate for H**).
- Individuals age 40-75 years with diabetes, and LDL-C 70-189 mg/dl without clinical ASCVD (**M if 10 yr risk <7.5%; H if ≥7.5%**).
- Individuals without clinical ASCVD or diabetes, who are age 40-75 years with LDL-C 70-189 mg/dl, and have an estimated 10-year ASCVD risk of **≥** 7.5% using Pooled Cohort Equations (**M or H**).

High- and Moderate-Intensity Daily Statin Therapy

- High Intensity (Lowers LDL-C ≥ 50%)
  - **Atorvastatin 40-80 mg**
  - **Rosuvastatin 20-**40 mg
- Moderate Intensity (Lowers LDL-C 30-50%)
  - **Atorvastatin 10** (20) **mg**
  - **Rosuvastatin** (5) **10 mg**
  - **Simvastatin 20–40 mg**
  - **Simvastatin 80 mg***
  - **Pravastatin 40** (80) **mg**
  - **Lovastatin 40 mg**
  - Fluvastatin XL 80 mg
  - **Fluvastatin 40 mg 2x/day**
  - Pitavastatin 2–4 mg

Bold = Tested in RCT and reviewed by Expert Panel
Orange= Not tested in RCT reviewed by Expert Panel

Efficacy of Intensive Lowering of LDL-C in Subjects with Low Baseline LDL-C

- Meta-analysis of RCT's of >1000 participants and ≥2 years treatment duration of more versus less intense statin trials involving 169,138 subjects
- The major vascular event reduction, among in those with baseline LDL-C <77mg/dL per further 39 mg/dL reduction was 29% (99% CI 2-48, p=0.007); in those with baseline LDL-C <70 mg/dl, similar reduction in LDL-C continued to demonstrate MVE reduction (RR 0.63, 99% CI 0.41-0.95, p=0.004).

Cholesterol Treatment Trialists Collaboration. Lancet 2010;376:1670-81

ACC/AHA Perspective on Statin Therapy

- Statin intensity trials showed clear benefit for high intensity versus moderate intensity statins
- Because fixed doses, not dosage titrations, were employed, one should not assume that a dosage titration strategy is correct or that addition of non-statins to achieve low LDL-C is indicated

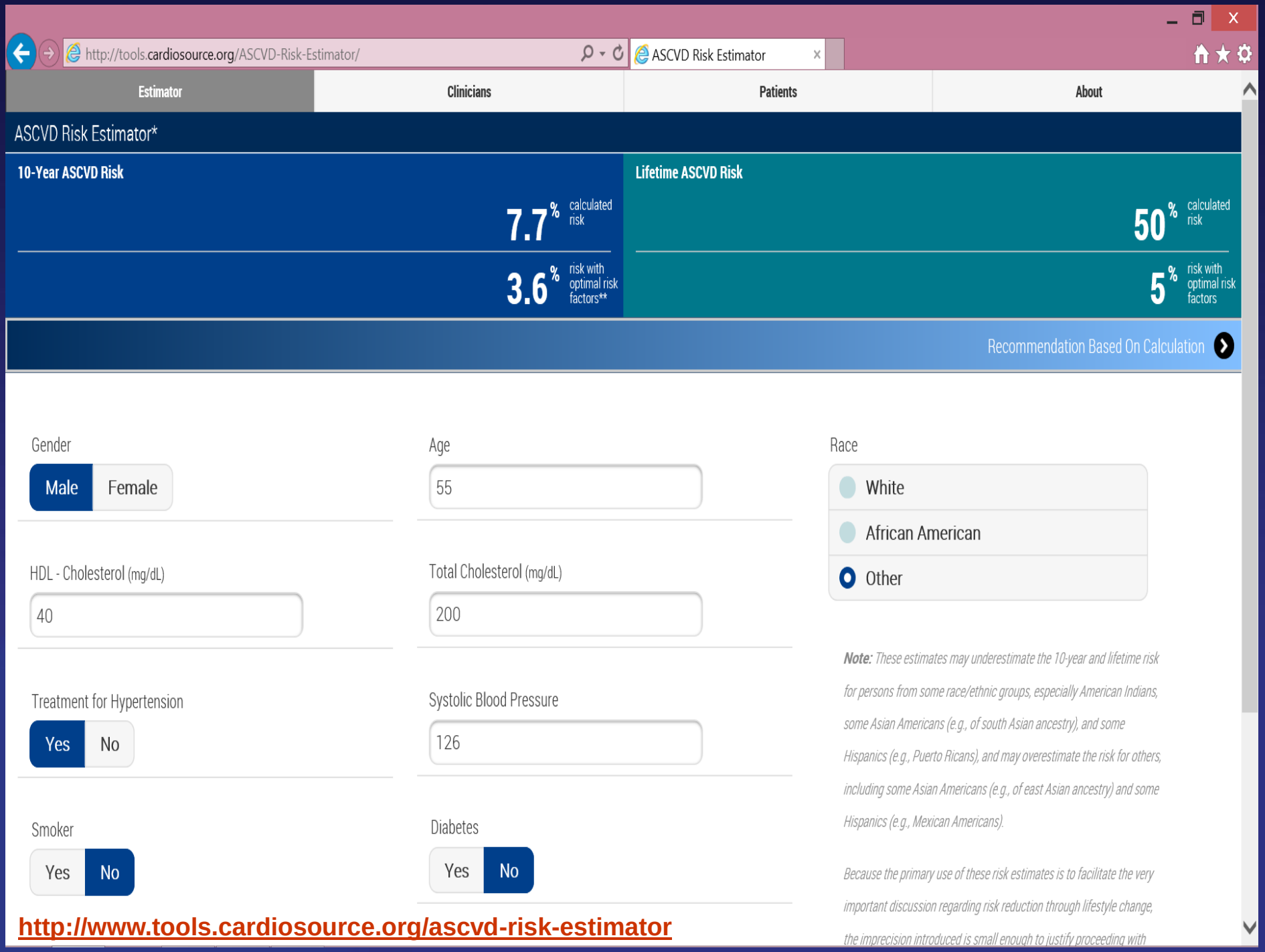
ACC/AHA Perspective on Non-Statin Lipid Drug Therapy

- Non-statin drugs without demonstrated ASCVD risk reduction may favorably alter lipids but have an unfavorable risk/benefit ratio
  - Niacin in AIM-HIGH and HPS-2 THRIVE
  - Fibrates in ACCORD-Lipid, FIELD
  - Lack of ASCVD event end-point data on ezetimibe
  - CETP inhibitors torcetrapib and dalcetrapib
- The use of non-statin drugs should generally be avoided

Risk Calculators

ACC/AHA

- Use Pooled Cohort Risk calculator in non-Hispanic Whites and non-Hispanic African Americans age 40-79 without ASCVD and not on statin therapy; may be considered in other populations
- Assessment of lifetime risk may be considered in those aged 20-59 with no ASCVD and not at high short-term risk

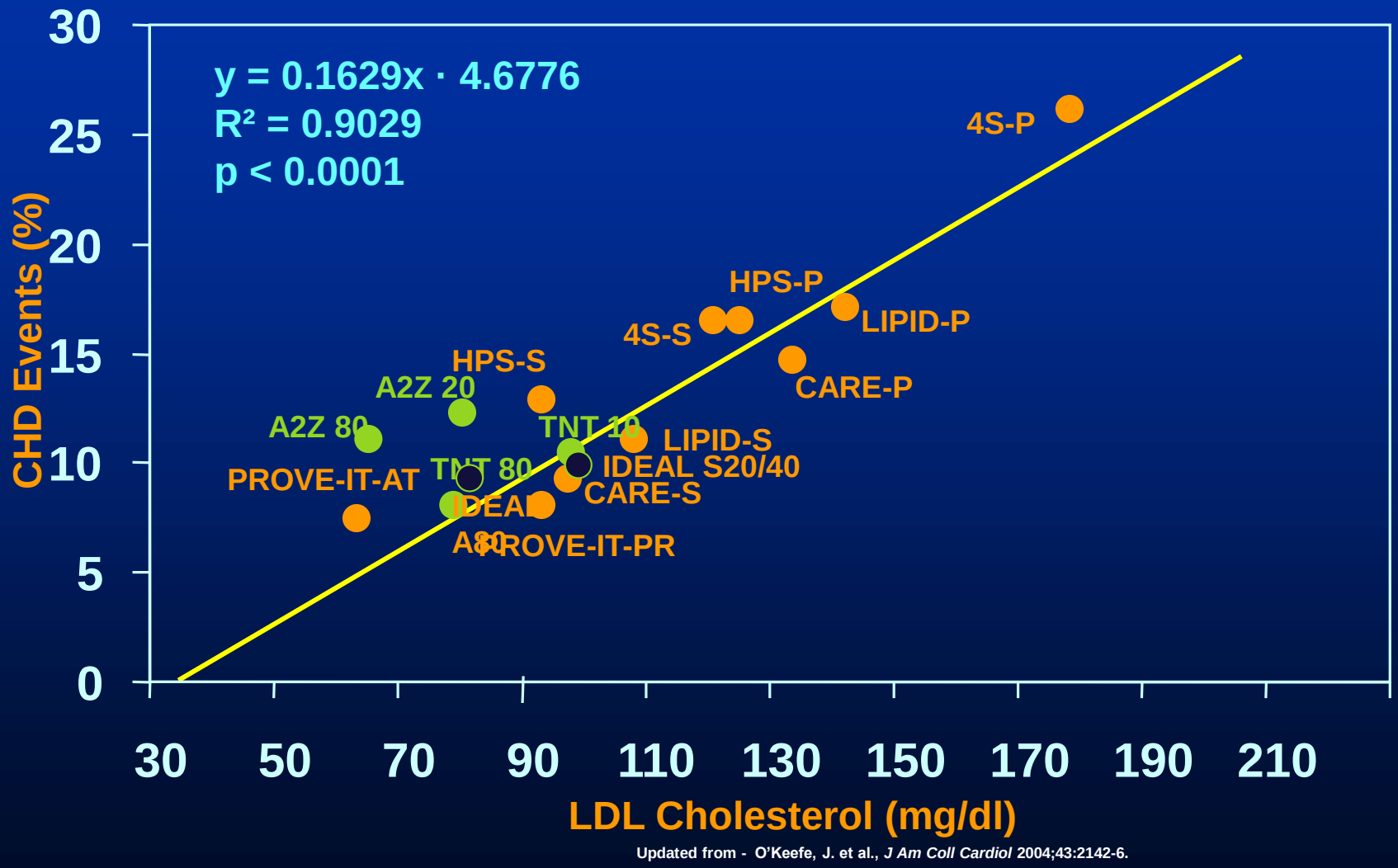


http://www.tools.cardiosource.org/ascvd-risk-estimator

ACC/AHA Risk Calculator: Possible Overtreatment in Older Patients?

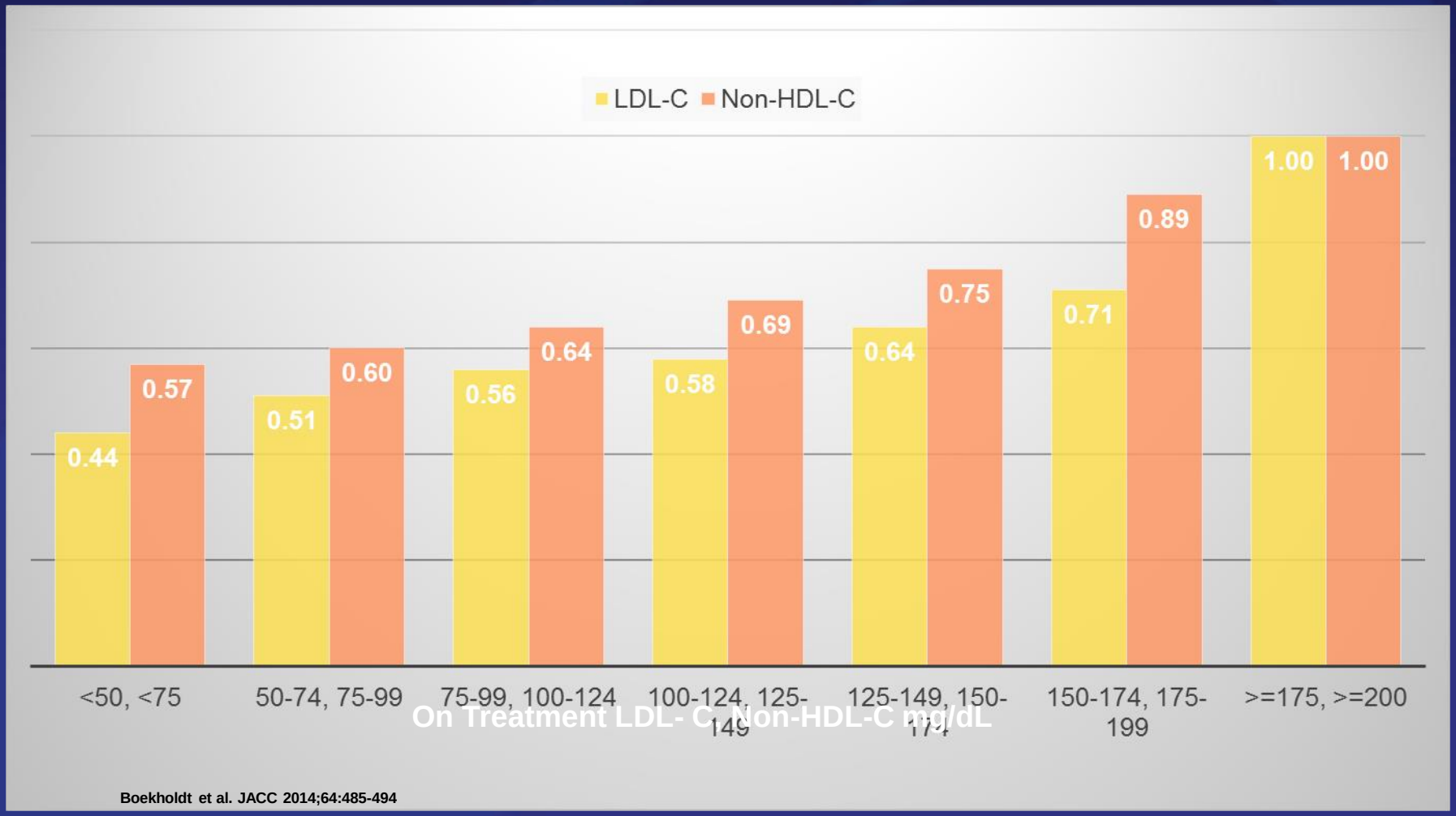
Age	Total cholesterol	HDL cholesterol	Systolic BP	Treatment for HBP	Diabetes	Smoker	10-year ASCVD risk
60 AA♂	170	50	125	No	No	No	7.5%
65 AA♀	178	50	130	No	No	No	7.5%
60 C ♂	170	47	125	No	No	No	7.5%

CHD Event Rates in Secondary Prevention and ACS Trials



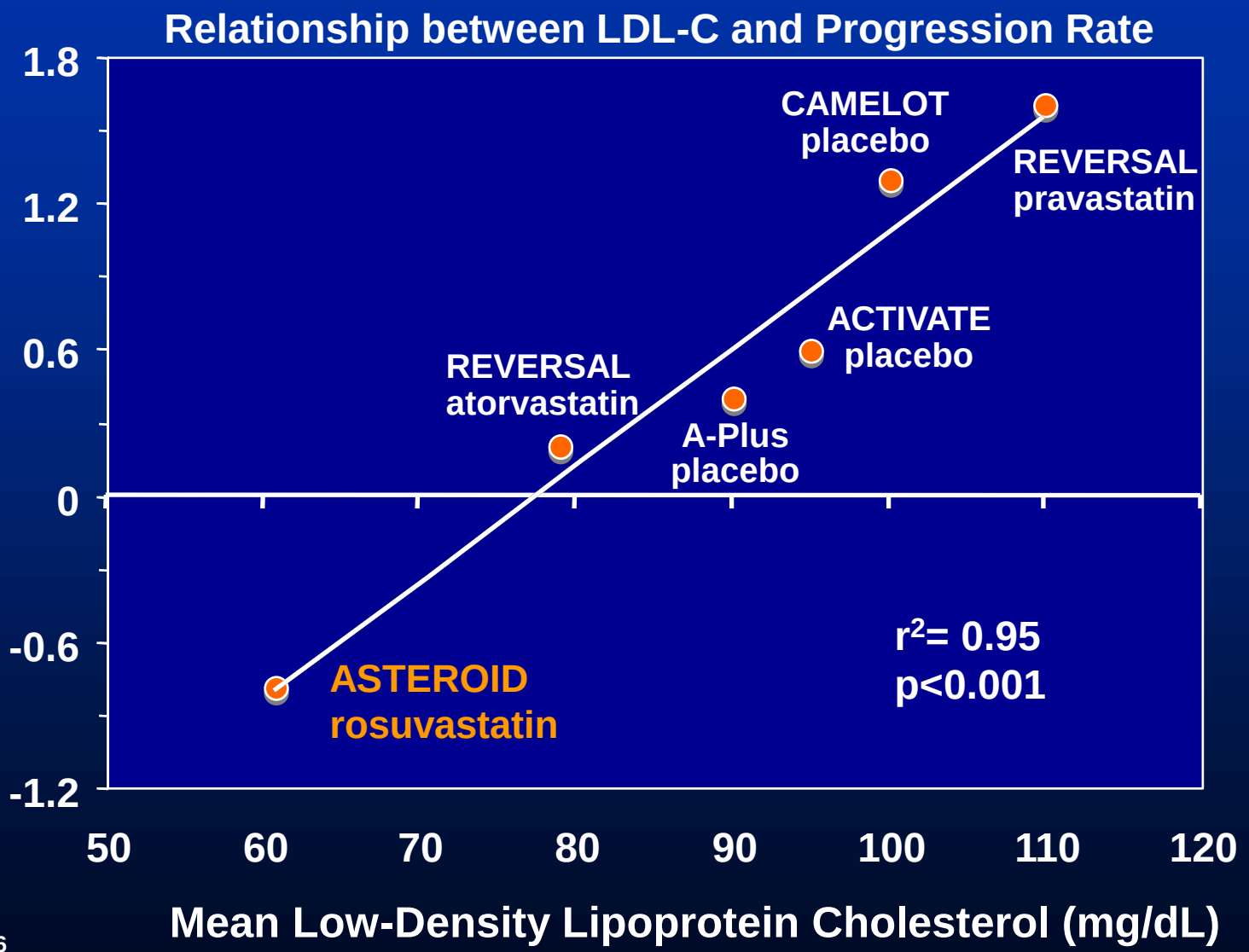
Updated from - O'Keefe, J. et al., *J Am Coll Cardiol* 2004;43:2142-6.

Very Low LDL-C and Non-HDL-C in Statin Trials and Major CVD Event Risk



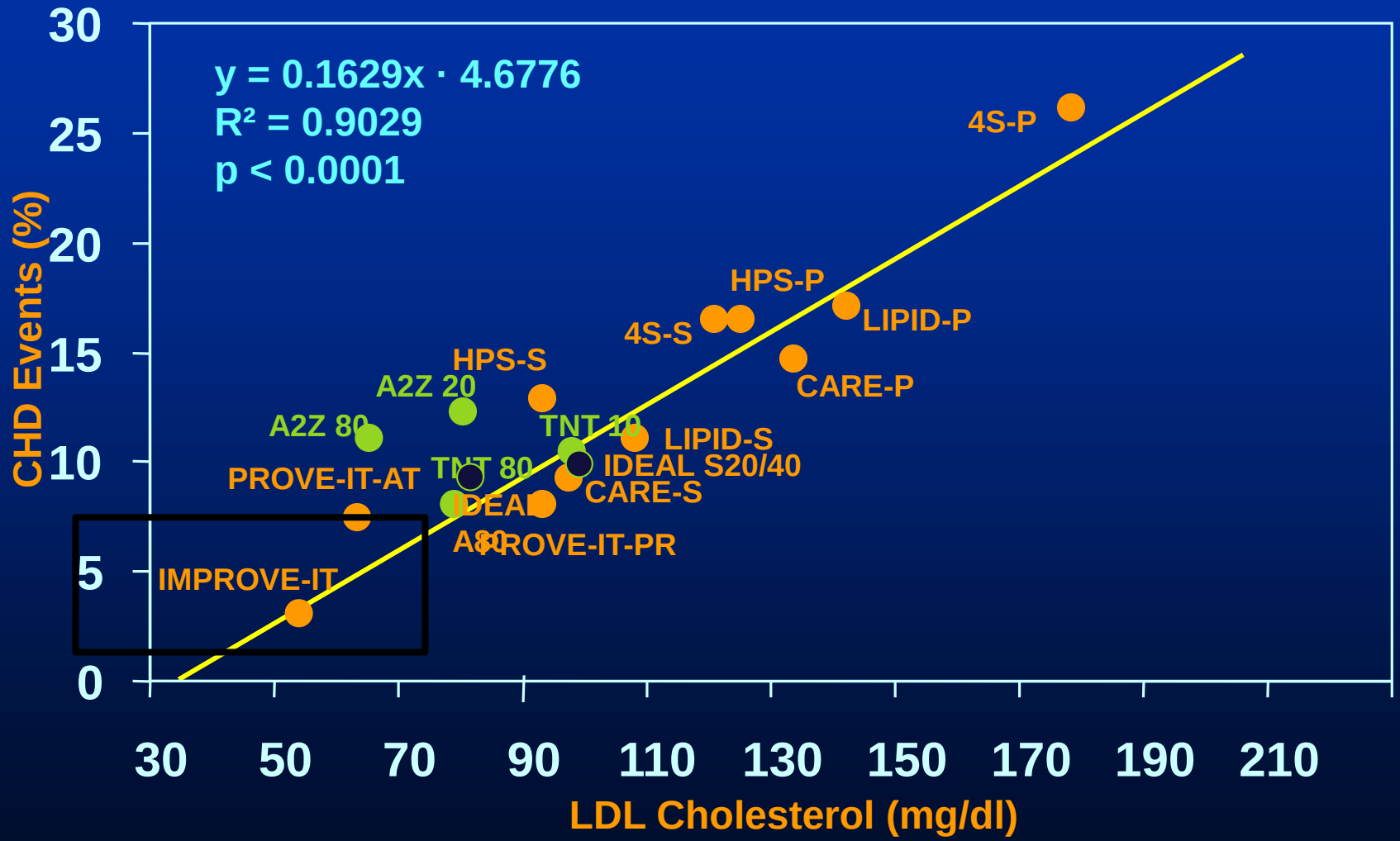
Boekholdt et al. JACC 2014;64:485-494

Recent Coronary IVUS Progression Trials



Nissen S. JAMA 2006

CHD Event Rates in Secondary Prevention and ACS Trials



Updated from - O'Keefe, J. et al., *J Am Coll Cardiol* 2004;43:2142-6.

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial

A Multicenter, Double-Blind, Randomized Study to Establish the Clinical Benefit and Safety of Vytorin (Ezetimibe/Simvastatin Tablet) vs Simvastatin Monotherapy in High-Risk Subjects Presenting With Acute Coronary Syndrome

National Lipid Association Guidelines

Overview of the NLA Recommendations

1. All preventive therapy begins with risk assessment and a provider-patient discussion of the pros and cons of therapy
2. Lifestyle therapy is at the basis of all ASCVD preventive recommendations, regardless of baseline risk
3. Judicious use of evidence-based drug therapy, particularly moderate and high-dose statins, is associated with optimal ASCVD risk reduction
4. When excessive circulating atherogenic cholesterol (non-HDL-cholesterol and LDL cholesterol) persists after appropriate lifestyle and statin therapy, the use of non-statin therapy may be considered
5. Long-term follow-up fostered by provider-patient communication is essential for optimal ASCVD prevention

Risk Category	Criteria
Very High	• ASCVD • Diabetes mellitus (type 1 or 2) ≥2 other major ASCVD risk factors; or Evidence of end-organ damage
High	• ≥3 major ASCVD risk factors • Diabetes mellitus (type 1 or 2) 0-1 other major ASCVD risk factor, and no evidence of end-organ damage • Chronic kidney disease Stage 3B or 4 • LDL-C ≥190 or non-HDL-C ≥220 mg/dL
Moderate	• 2 major ASCVD risk factors • For specific clinical features, high quantitative risk score or specific biomarker levels, consider reclassification to high risk
Low	• 0-1 major ASCVD risk factor • For specific clinical features, consider reclassification to moderate risk

NLA ASCVD Risk Categories, Levels for Consideration of Drug Therapy and Treatment Goals

Risk Category	Consider Drug Therapy	Treatment Goal
	Non-HDL-C /LDL-C Goal (mg/dL)	Non-HDL-C/LDL-C Goal (mg/dL)
Very-high	≥100 ≥70	<100 <70
High	≥130 ≥100	<130 <100
Moderate	≥160 ≥130	<130 <100
Low	≥190 ≥160	<130 <100

For patients with ASCVD or diabetes mellitus, consider use of moderate or high intensity statins, irrespective of baseline atherogenic cholesterol levels.

NLA Perspective on Statin Therapy

- Statin therapy is the most potent and evidence-based approach to lowering atherogenic lipoproteins (non-HDL-C and LDL-C)
- Statin intensity trials showed clear benefit for high-intensity versus moderate-intensity statins
- Broad-based evidence supports "lower is better" concept, and provides an opportunity for clinicians to address residual risk above that addressed by appropriately-dosed statin therapy

NLA Perspective on Non-Statin Lipid Drug Therapy

- If non-HDL-C and LDL-C goals are not achieved with maximal tolerated statin therapy, the addition of non-statin therapy should be considered to lower atherogenic cholesterol levels and to achieve goals
  - Doctors can be instructed not to use niacin in patients on aggressive statin regimens
  - As ezetimibe is safe and lowers atherogenic cholesterol, its use may be considered in selected patients with elevated non-HDL-C and/or LDL-C
  - Resins may be considered in selected patients
  - Meta-analyses of fibrate therapy in subgroups with atherogenic dyslipidemia suggest ASCVD risk reduction

Evidence Base: Summary

- ACC/AHA
  - By limiting the scope to RCT of statins and meta-analyses of RCT, only the highest level of evidence on statins in defined populations is employed to assess ASCVD outcomes
- NLA
  - By including evidence from RCT and other sources, a broader evidence base for clinical decision making is employed. This approach is consistent with the perspective of previous NCEP ATP's and the international community

Lipid Guideline Controversies: Common Threads Between ACC/AHA and NLA

- Lifestyle therapy is warranted for ASCVD risk reduction, whether or not drug therapy is used
- Patients with ASCVD, FH and diabetes are candidates for moderate or high-dose statins
- Risk calculators aid in, but do not take the place of clinical judgment
- Whether or not lipid goals are set, regular lipid follow-up is warranted to assess adherence
- Patient engagement in preventive care decision making aids in long-term adherence

Current problem

Despite the widespread availability of statins, many patients fail to reach recommended LDL-C targets in clinical practice, even in combination with other lipid lowering agents and are unable achieve an LDL < 70 mg/dl.

Numerous patients are often intolerant to statins and or high intensity statins due to various side effects (muscle aches, etc.)

Emerging Therapies
PCSK9 Inhibitors

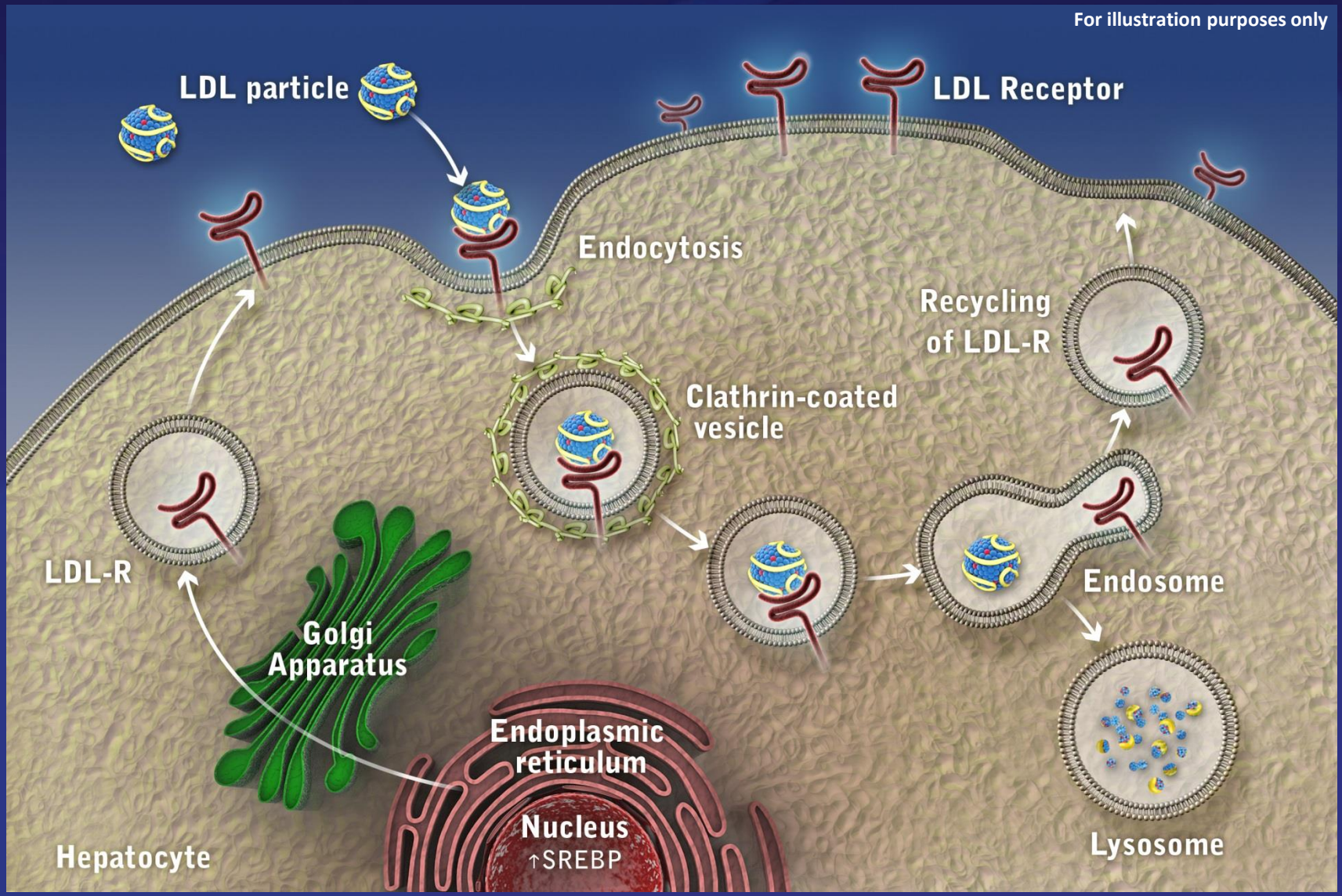
Background: PCSK9 Inhibition

- PCSK 9 inhibitors are fully human monoclonal antibodies against PCSK9 which reduced LDL-C by up to 65% and was well tolerated in multiple randomized, placebo-controlled, phase 2 clinical trials of 12 weeks duration in over 1300 hypercholesterolemic patients.[1-4]

- The PCSK9 inhibitors are a new class of drugs that have been shown to dramatically lower LDL cholesterol levels. PCSK9 inhibitors are monoclonal antibodies (MABs). They inactivate a protein in the liver called proprotein convertase subtilisin kexin 9 (PCSK9). PCSK9 itself inactivates the needed receptors on the liver cell surface that transport LDL into the liver for metabolism (break down). Without these receptors, more LDL ("bad" cholesterol) remains in the blood. So, by inactivating PCSK9 via inhibition, more receptors are available to capture LDL for metabolism and removal from the blood.(5)

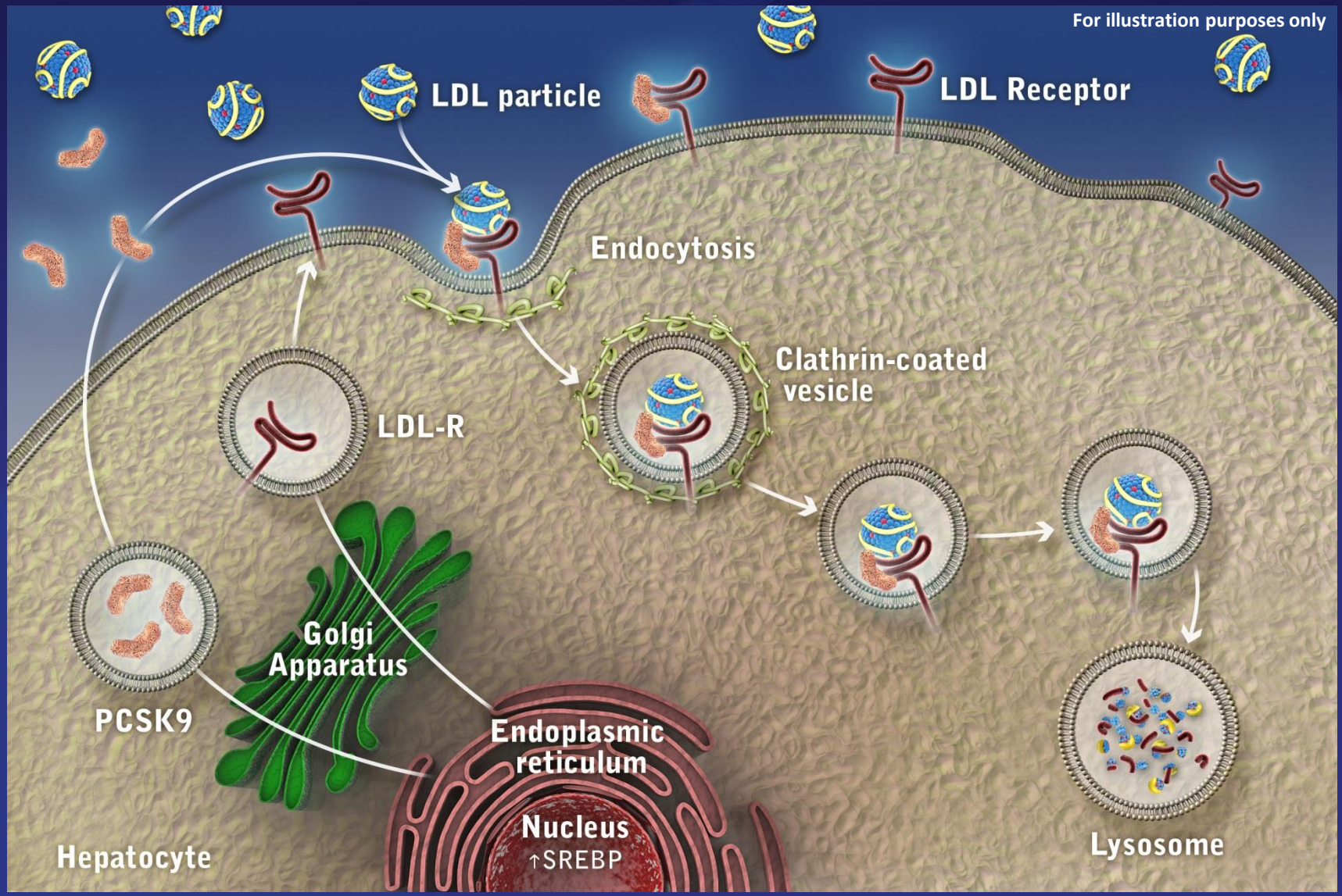
1. ***Lancet*. 2012;380:1995-2006**
2. ***Circulation*. 2012;126:2408-2417**
3. ***JAMA*. 2012;308:2497-2506**
4. ***Lancet*. 2012;380:2007-2017**
5. ***http://www.drugs.com/slideshow/pcsk9-inhibitors-a-new-option-in-cholesterol-treatment-1166#slide-2***

LDL Receptor Function and Life Cycle



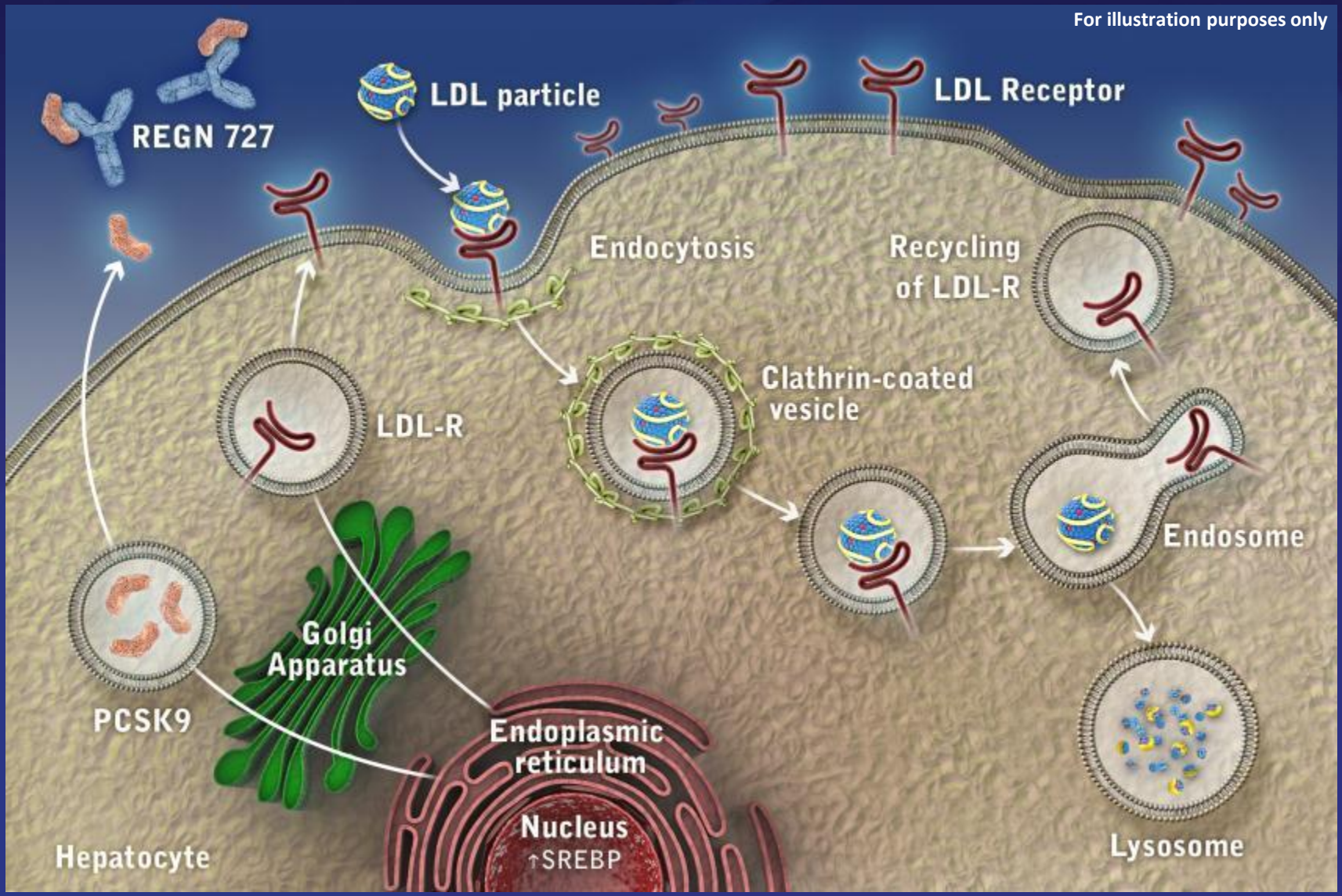
Clinicaltrials.gov no. NCT01288443

The Role of PCSK9 in the Regulation of LDL Receptor Expression



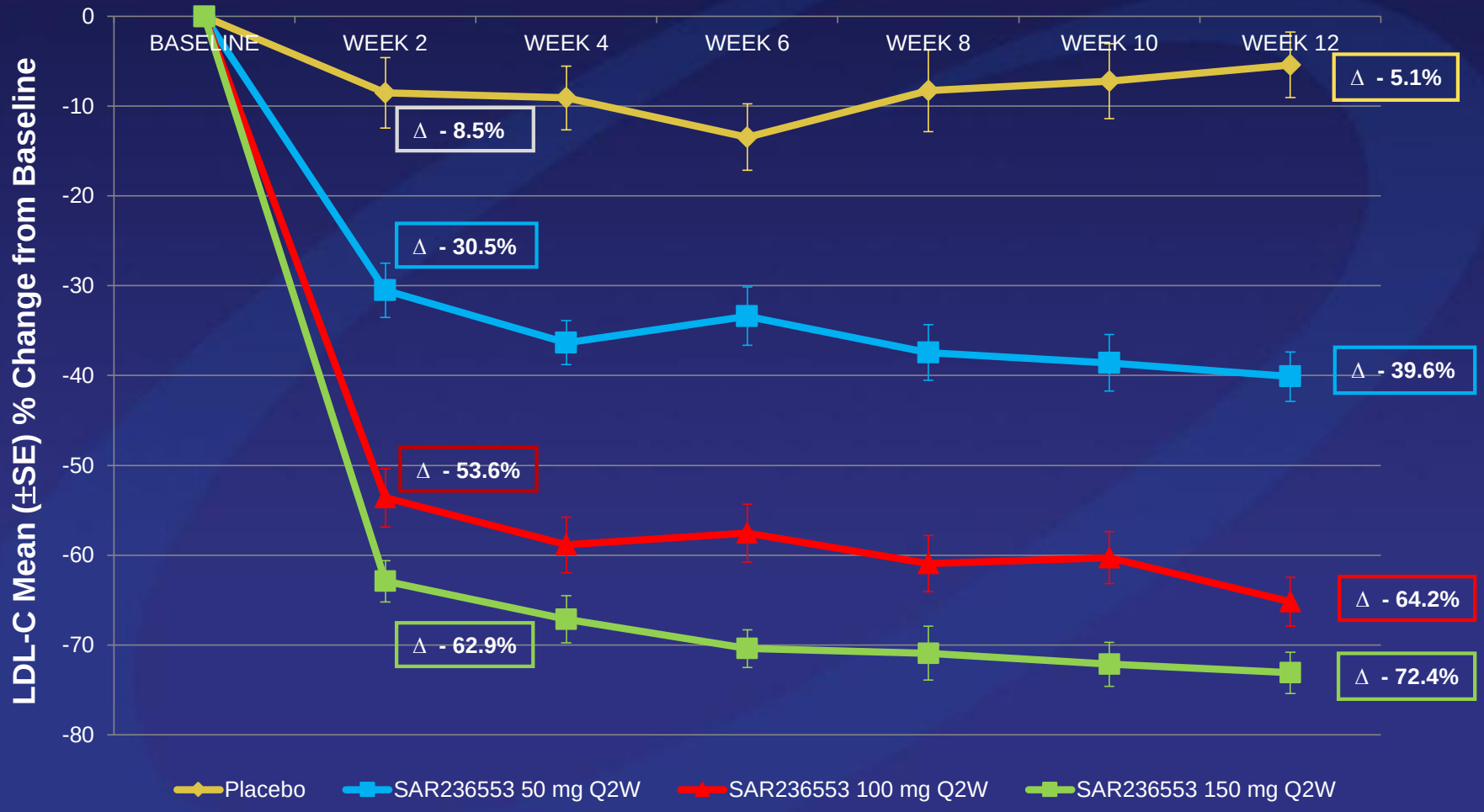
Clinicaltrials.gov no. NCT01288443

Impact of an PCSK9 mAb on LDL Receptor Expression



Clinicaltrials.gov no. NCT01288443

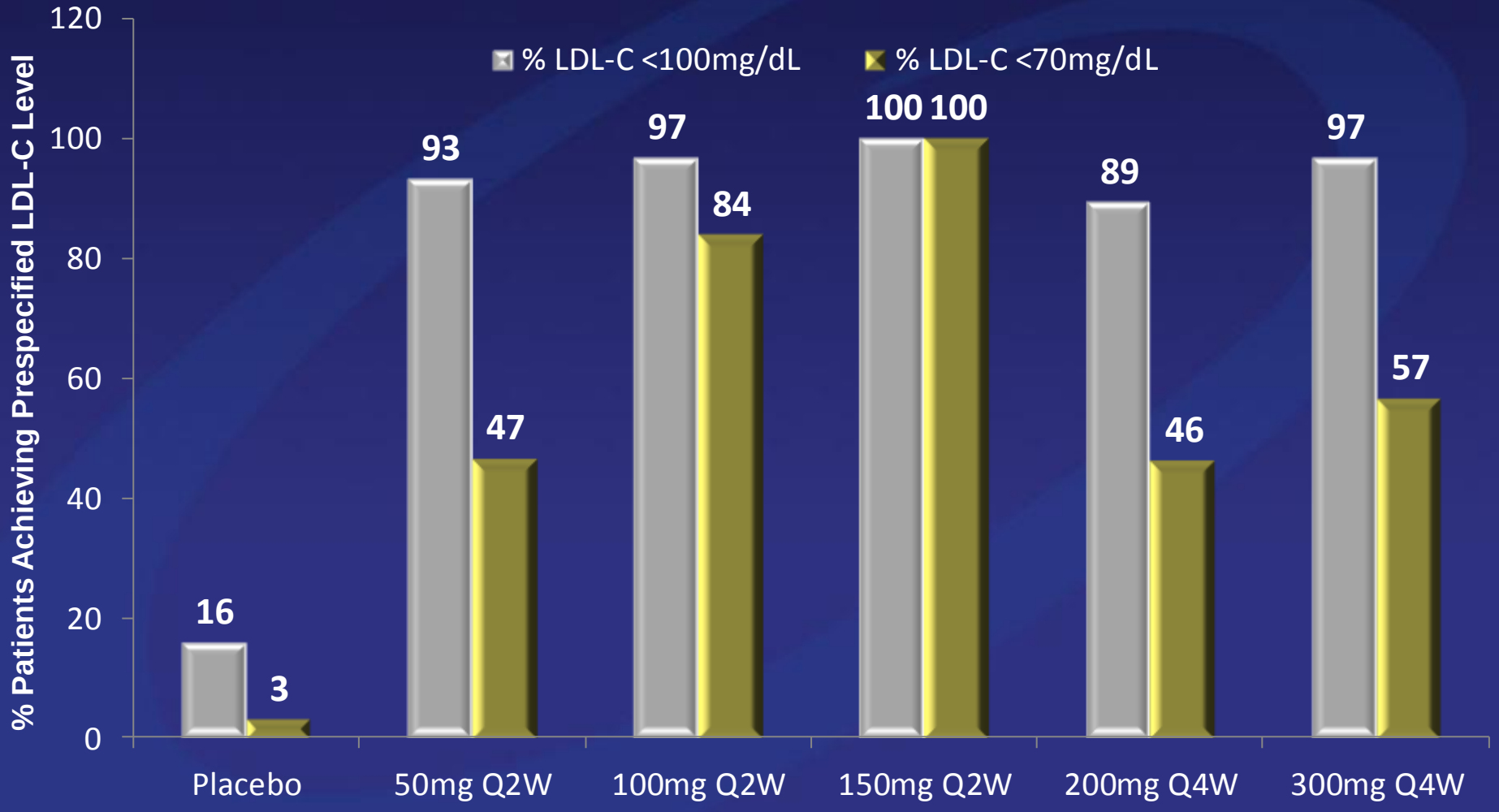
Change in Calculated LDL-C at 2 Weekly Intervals from Baseline to Week 12



Mean percentage change in calculated LDL-C from baseline to weeks 2, 4, 6, 8, 10, and 12 in the modified intent-to-treat (mITT) population, by treatment group. Week 12 estimation using LOCF method.

Clinicaltrials.gov no. NCT01288443

Attainment of Prespecified LDL-C Levels at Week 12 (mITT Population)



Clinicaltrials.gov no. NCT01288443

Changes in TG, HDL-C, and Apo AI from Baseline to Week 12 by Treatment Group (mITT Population)

[1]LS mean (SE)
[2]median (Q1-Q3)

Clinicaltrials.gov no. NCT01288443

Summary of Treatment-Emergent Adverse Events (TEAEs) (Safety Population)

		Q2W dosing			Q4W dosing	
	Placebo (N=31)	50mg (N=30)	100mg (N=31)	150mg (N=31)	200mg (N=30)	300mg (N=30)
Overview of all TEAEs – no.						
Any TEAE	14	18	20	19	20	14
Any treatment-emergent SAE	1	0	1	0	1	1
Any TEAE leading to permanent treatment d/c	0	0	1	1	3	1
AEs of special interest — no.						
ALT or AST >3 x ULN	0	0	0	0	0	0
Muscle (including pain, weakness)	1	1	2	1	1	2
CK >10 x ULN	1	0	0	0	0	0

Injection-site reactions occurred in the SAR236553 groups only and were generally mild and non-progress

Clinicaltrials.gov no. NCT01288443

Summary and Conclusions

- PCSK9 inhibitors produced significant, dose-dependent LDL-C reductions
  - Up to 72% LDL-C reduction with 150mg Q2W
  - Improved ability to achieve LDL-C goal cut points
  - LDL-C reductions were generally unaffected by baseline atorvastatin dose
- Consistent and robust reductions for all other Apo B–containing lipoproteins
  - Important reduction in Lp (a), consistent with prior studies
- Trend towards decreases in TG and increases in HDL-C and Apo AI vs placebo
- PCSK9 inhibitors are well tolerated
- No signals for persistent or prevalent clinical or laboratory adverse events including hepatic and muscle assessments.

Clinicaltrials.gov no. NCT01288443

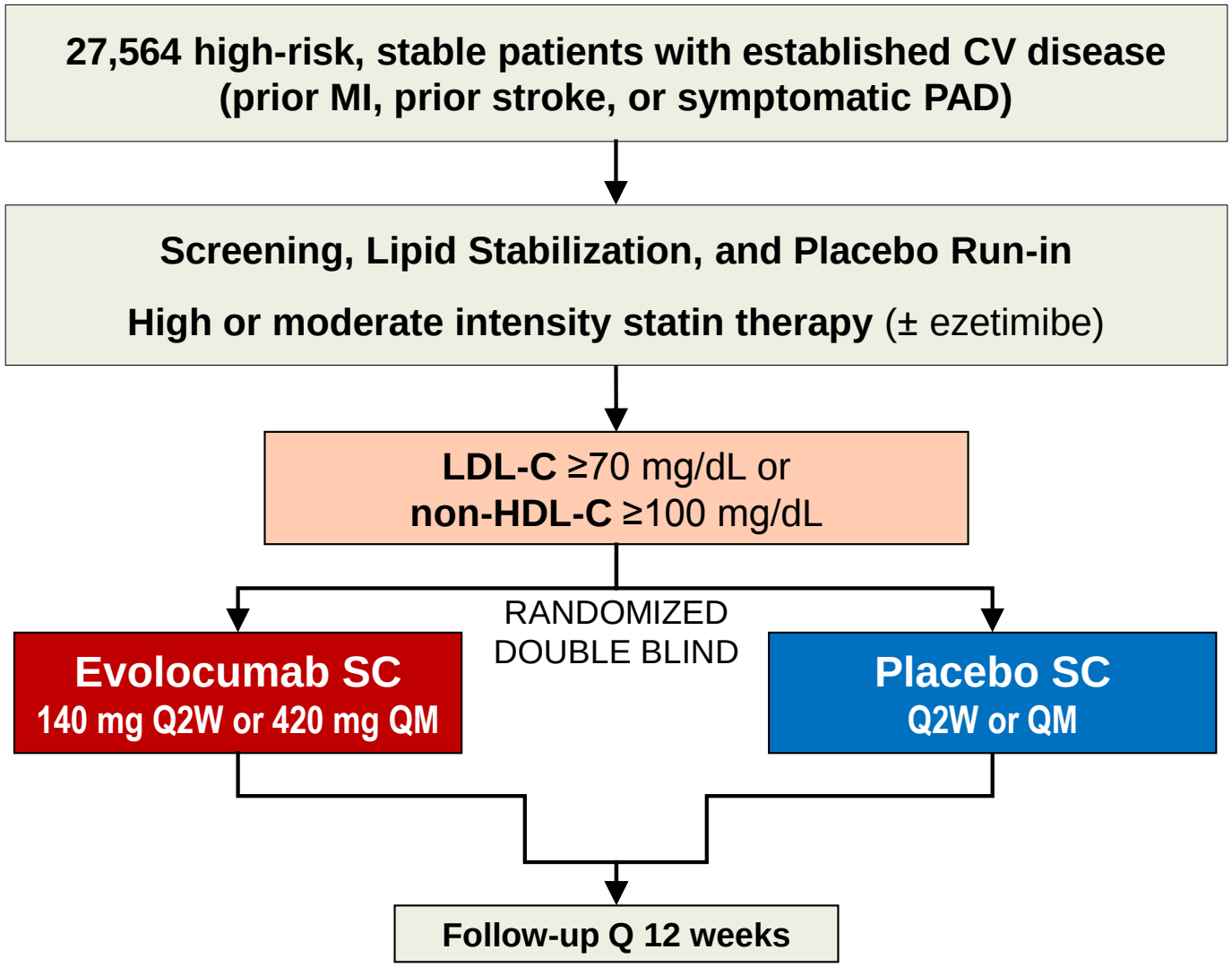
Further Details

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., Narimon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, M.A., Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

Article available at www.nejm.org
Slides available at www.TIMI.org

Trial Design



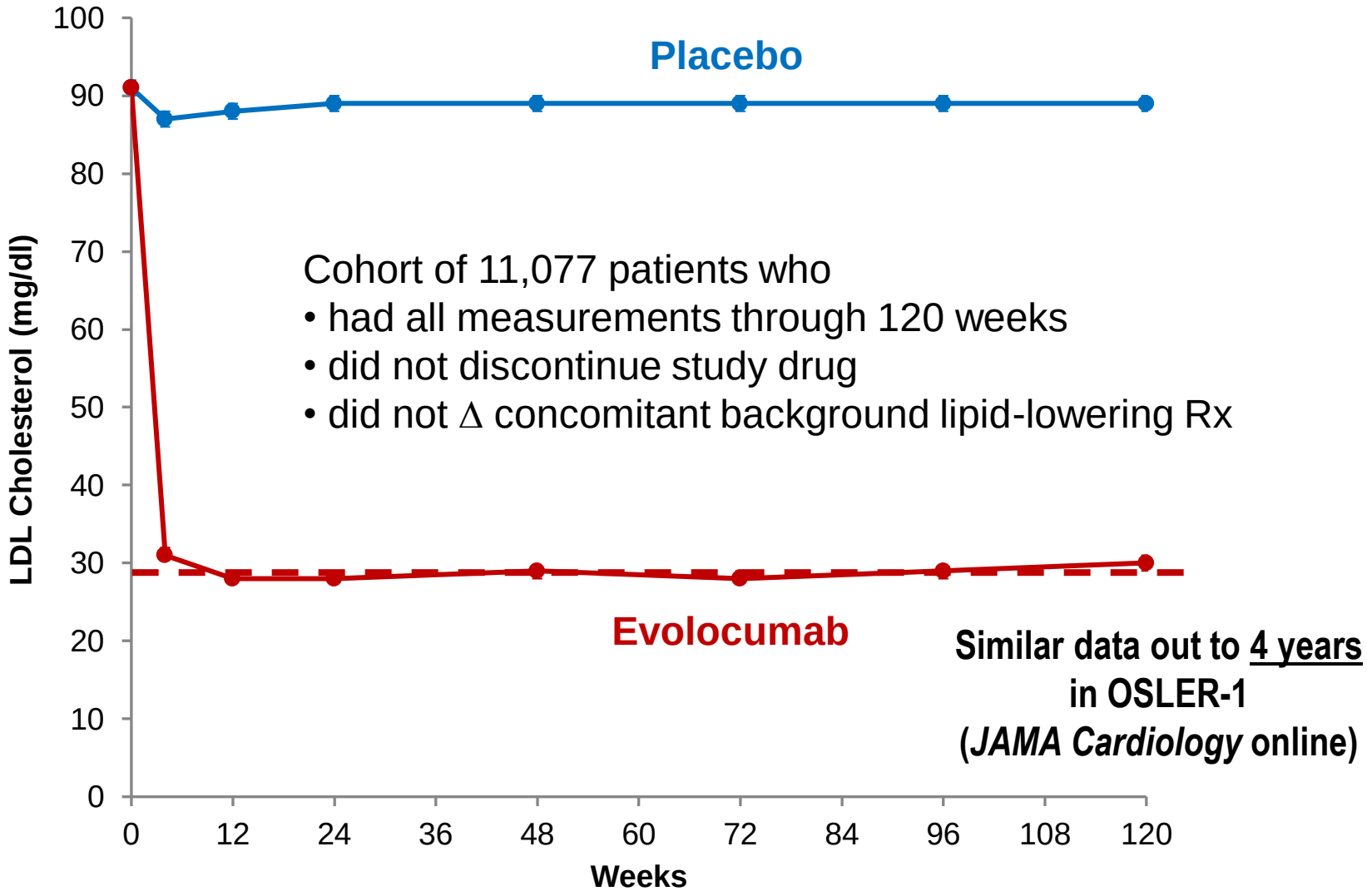
Sabatine MS et al. *Am Heart J* 2016;173:94-101

Endpoints

- **Efficacy**
  - **Primary: CV death, MI, stroke, hosp. for UA, or coronary revasc**
  - **Key secondary: CV death, MI or stroke**
- **Safety**
  - **AEs/SAEs**
  - **Events of interest incl. muscle-related, new-onset diabetes, neurocognitive**
  - **Development of anti-evolocumab Ab (binding and neutralizing)**
- **TIMI Clinical Events Committee (CEC)**
  - **Adjudicated all efficacy endpoints & new-onset diabetes**
  - **Members unaware of treatment assignment & lipid levels**

Sabatine MS et al. *Am Heart J* 2016;173:94-101

LDL Cholesterol

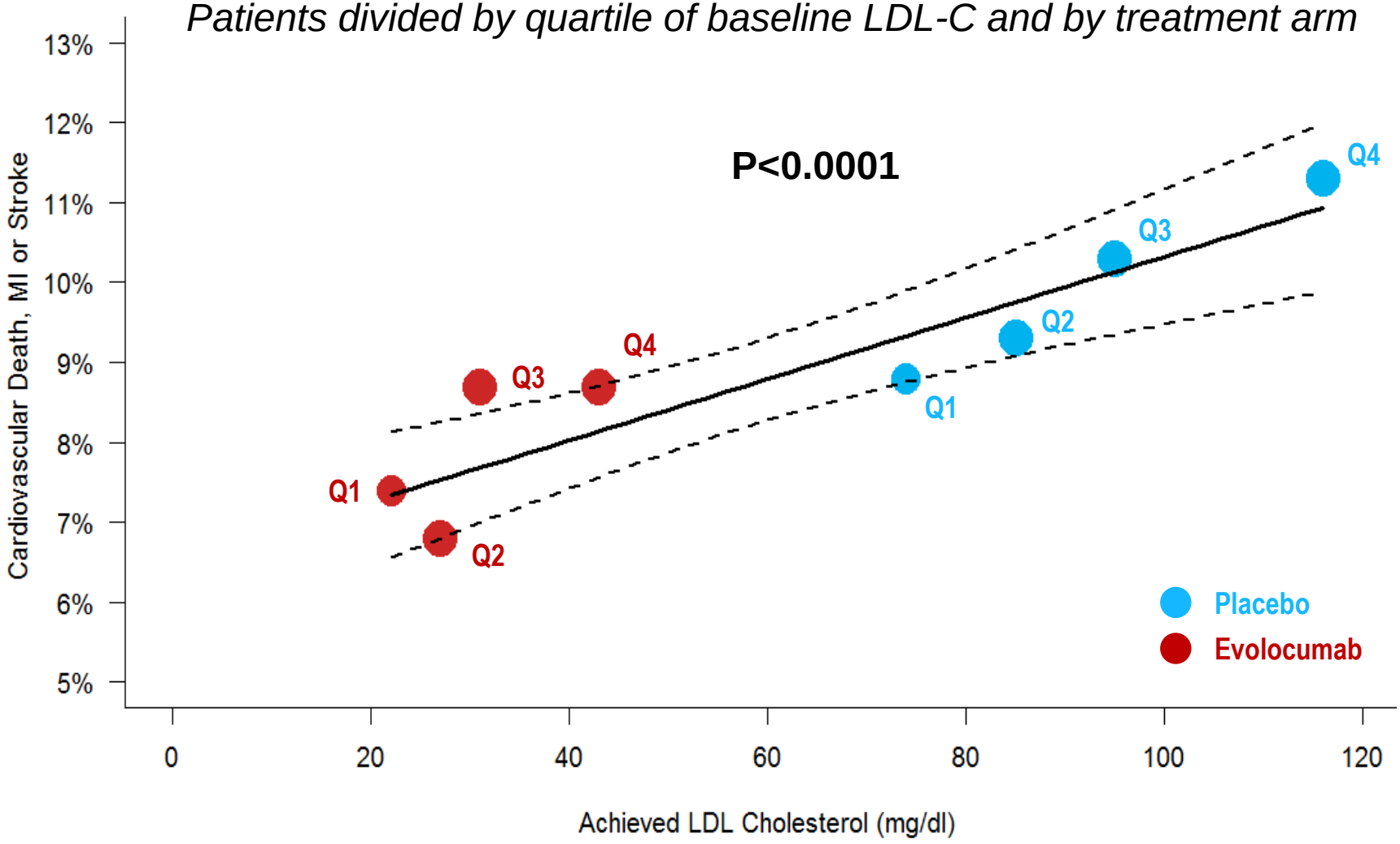


Cohort of 11,077 patients who
- had all measurements through 120 weeks
- did not discontinue study drug
- did not Δ concomitant background lipid-lowering Rx

Similar data out to 4 years in OSLER-1 (*JAMA Cardiology* online)

Lower LDL-C Is Better

Patients divided by quartile of baseline LDL-C and by treatment arm



Safety

	Evolocumab (N=13,769)	Placebo (N=13,756)
Adverse events (%)		
Any	77.4	77.4
Serious	24.8	24.7
Allergic reaction	3.1	2.9
Injection-site reaction	2.1	1.6
Treatment-related and led to d/c of study drug	1.6	1.5
Muscle-related	5.0	4.8
Cataract	1.7	1.8
Diabetes (new-onset)	8.1	7.7
Neurocognitive	1.6	1.5
Laboratory results (%)		
Binding Ab	0.3	n/a
Neutralizing Ab	*none*	n/a

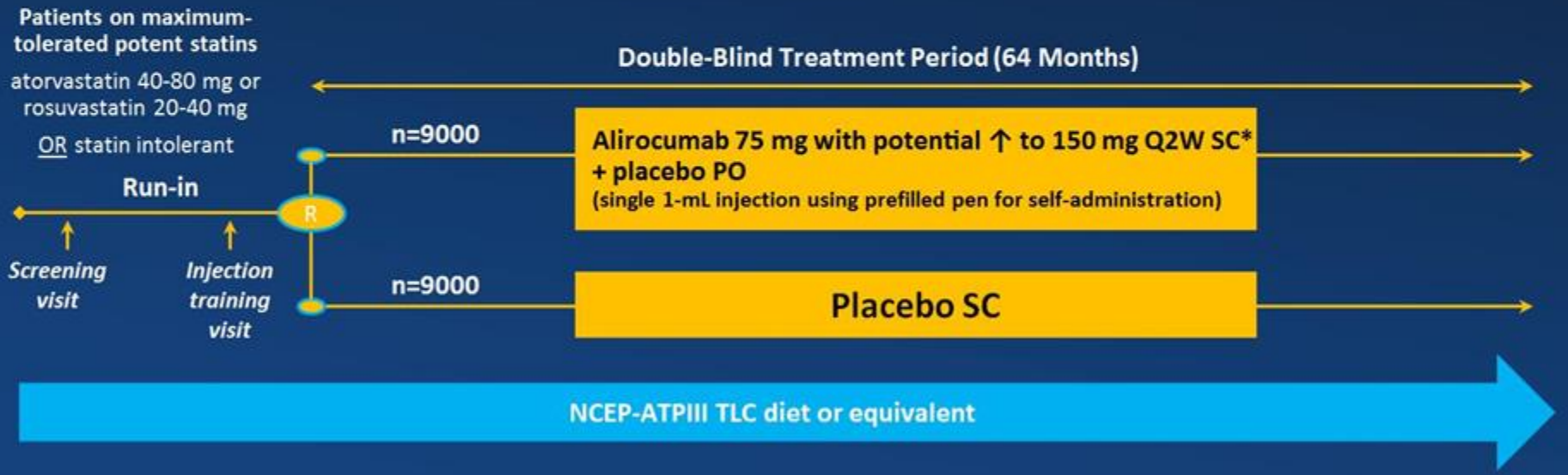
New-onset diabetes assessed in patients without diabetes at baseline; adjudicated by CEC

Summary for Evolocumab

- **↓ LDL-C by 59%**
  - Consistent throughout duration of trial
  - Median achieved LDL-C of 30 mg/dl (IQR 19-46 mg/dl)
- **↓ CV outcomes in patients already on statin therapy**
  - 15% ↓ broad primary endpoint; 20% ↓ CV death, MI, or stroke
  - Consistent benefit, incl. in those on high-intensity statin, low LDL-C
  - 25% reduction in CV death, MI, or stroke after 1st year
  - Long-term benefits consistent w/ statins per mmol/L ↓ LDL-C
- **Safe and well-tolerated**
  - Similar rates of AEs, incl DM & neurocog events w/ EvoMab & pbo
  - Rates of EvoMab discontinuation low and no greater than pbo
  - No neutralizing antibodies developed

ODYSSEY OUTCOMES – Study Design

Population	Lipid criteria at entry	Primary endpoint
• Patients 4-52 weeks post-ACS • Age ≥ 40	• LDL-C ≥70 mg/dL [≥1.81 mmol/L] OR • ApoB ≥80 mg/dL [≥0.8 mmol/L] OR • Non-HDL-C ≥100 mg/dL [≥2.59 mmol/L]	• Composite of – CHD death – Nonfatal MI – Ischemic stroke – High-risk UA requiring hospitalization



ACS=acute coronary syndrome; CHD=coronary heart disease; LDL-C=low-density lipoprotein cholesterol; MI=myocardial infarction; Q2W=every other week; SC=subcutaneous; TLC=therapeutic lifestyle changes; UA=unstable angina.

*Dose titrated up to 150mg Q2W at Month 2 if LDL-C ≥50 mg/dL(1.29 mmol/L) at Month 1 visit.

ClinicalTrials.gov. ODYSSEY OUTCOMES Study. http://clinicaltrials.gov/ct2/show/NCT01663402. Accessed May 14, 2015.
Schwartz GG, et al. *Am Heart J*. 2014;168:682-689.e1.

CASE STUDIES

Patient Case #2

- 75 year old African American male with a history of CABG x 3 in 2010 and HTN presents to your office for a routine physical examination

- Medications: metoprolol XL100 mg daily, losartan 50 mg daily and aspirin 81 mg daily

- Lipid Profile: TC 180 mg/dl, LDL-C 90 mg/dl, HDL-C 40 mg/dl, TG 200 mg/dl, LFTs NL

Patient Case #2

Which therapy if any would you institute in this patient?

(75 yo, CAD- TC 180 mg/dl, LDL-C 90 mg/dl, HDL-C 40 mg/dl, TG 200 mg/dl)

- A. Pravastatin 20 mg daily
- B. Rosuvastatin 20 mg daily
- C. Atorvastatin 40 mg daily
- D. Lovastatin 20 mg daily
- E. Alirocumab 75 mg 2x monthly
- F. No Statin therapy is indicated. Continue diet and exercise.

Patient Case #3

- 40 year old Caucasian female with a history of DM and HTN presents to your office for a routine physical examination. Calculated Global Risk Index is 9%.

- Medications: vasotec 20 mg daily and aspirin 81 mg daily

- Lipid Profile: TC 180 mg/dl, LDL-C 100 mg/dl, HDL-C 50 mg/dl, TG 150 mg/dl, LFTs NL

Patient Case #3

Which therapy (if any) would you institute in this patient?

(40, DM, global risk index 9%- TC 180 mg/dl, LDL-C 100 mg/dl, HDL-C 50 mg/dl, TG 150 mg/dl)

- A. Pravastatin 40 mg daily
- B. Rosuvastatin 20 mg daily
- C. Atorvastatin 40 mg daily
- D. Lovastatin 20 mg daily
- E. Alirocumab 75 mg 2x monthly
- F. No Statin therapy is indicated. Continue primary prevention strategies.

Patient Case #4

- 55 year old male with a history of CAD noted on cardiac catheterization in 2008 presents to your office for a routine physical examination

- Medications: allopurinol 100 mg daily, losartan 50 mg daily, atorvastatin 40 mg and synthroid 75 mcg daily

- Lipid Profile: TC 170 mg/dl, LDL-C 90 mg/dl, HDL-C 50 mg/dl, TG 150 mg/dl, LFTs NL

Patient Case #4

Which treatment plan would you institute in this patient?

- A. Increase atorvastatin to 80 mg daily
- B. Continue atorvastatin 40 mg daily
- C. Continue atorvastatin 40 mg daily and add ezetimide 10 mg daily
- D. Add Alirocumab 75 mg 2x monthly
- E. Discontinue atorvastatin and start rosuvastatin 40 mg daily
- F. Consult TCI Cardiology

Patient Case #5

- 72 year old female with a history of CAD, PVD and DM presents to your office for a routine follow-up. He has been intolerant to atorvastatin, rosuvastatin, simvastatin, pravastatin and pitvastatin due to muscle aches.

- Medications: aspirin 81 mg daily, Lisinopril 10 mg daily, amlodipine 10 mg daily and Coenzyme Q 10

- Lipid Profile: TC 200 mg/dl, LDL-C 120 mg/dl, HDL-C 50 mg/dl, TG 150 mg/dl, LFTs NL

Patient Case #5

Which therapy if any would you institute in this patient?

- A. ezetimibe 10 mg daily
- B. alirocumab 75 mg SQ 2 x monthly
- C. alirocumab 75 mg SQ 2 x monthly and ezetimide 10 mg daily
- D. alirocumab 150 mg SQ 2 x monthly
- E. None of the above (different therapy).
- F. No Statin therapy is indicated.

Final Thoughts

- For patients with established CAD, the recommended goal is < 70 mg/dl (ideal 40-60 mg/dl? To be determined).
- ATP IV may be beneficial in treating primary prevention patients that may not otherwise be candidates for statin therapy.
- What is the ideal LDL target for patients with CAD? How low is too low?
- Awaiting outcomes trial data from Odyssey Outcomes Study due in 2017 in patients on a PCSK9 inhibitor.

Thank you!

References

Sitbon O *et al. Circulation* 2005
D'Alonzo GE *et al*. *Ann Intern Med* 1991
Galie N *et al*. *Eur Heart J* 2004.
Gaine SP *et al. Lancet* 1998
Barst RJ *et al. J Am Coll Cardiol* 2004
Simonneau G *et al. JACC* 2004
Barst RJ *et al. J Am Coll Cardiol* 2004
D'Alonzo GE, et al. Ann Intern Med 1991;115:343-349.
Peacock AJ. *BMJ* 2003
Gaine SP *et al. Lancet* 1998
Sitbon O *et al*. *Am J Resp Crit Care Med* 2008
Lin EE *et al*. *Curr Hematol Rep* 2005
McGoon M *et al. Chest* 2004
Stewart DJ *et al. Ann Inter Med* 1991
Vancheeswaran R *et al. J Rheum* 1994
Yoshibayashi M *et al*. *Circulation* 1991
Galiè N *et al. Eur J Clin Invest* 1996
Channick RN *et al*. *Lancet* 2001
Kato I *et al*. *Cancer* 2001
Bjoraker JA *et al*. *Am J Respir Crit Care Med* 1998
Humbert M *et al*. *Am J Respir Crit Care Med* 2006
Sitbon O *et al*. *J Am Coll Cardiol* 2002
Galie N *et al*. *Eur Heart J* 2004
Hachulla E *et al Ann Rheum Dis* 2004
McGoon M *et al*. *Chest* 2004
ATS. *Am J Crit Care Med* 2002
Galiè N *et al*. *Lancet* 2008
Humbert H *et al. N Engl J Med* 2004
Channick RN *et al. Lancet* 2001
Humbert H *et al. N Engl J Med* 2004
Galiè N *et al. N Engl J Med* 2005