

How Thick is too Thick for Your Arteries?

Ezetimibe versus niacin for cardiovascular risk reduction

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The authors have no disclosures or conflicts of interest to report.

A cornerstone of cardiovascular risk reduction has focused on the management of cholesterol, with particular focus on low-density lipoproteins (LDL-C). The atherogenicity of LDL-C has been established through multiple epidemiological studies and subsequent population studies, including The Framingham Heart Study, the Multiple Risk Factor Intervention Trial (MRFIT), and the Lipid Research Clinics (LRC) trial. These trials have noted direct correlation between increased levels of LDL-C and the rate of Coronary Heart Disease (CHD).¹⁻⁵ HMG-CoA reductase inhibitors (statins) have long been the drug of choice for reduction of LDL-C. Meta-analysis has shown that over approximately a 5-year period, the utilization of statin therapy can reduce major coronary events and all-cause mortality by 31% and 21%, respectively.⁶ Many patients can reach their lipid goals through utilization of a statin medication. Most recently, the Heart Protection Study (HPS) and Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolytic in Myocardial Infarction Study (PROVE-IT) noted in patients with a high risk of coronary events, intensified statin dosing provided greater protection against mortality or cardiovascular events.⁷⁻⁸

However, there remains the clinical question, when patients are not meeting their LDL-C goals on statin monotherapy, which lipid lowering agent should be used as a second-line for further cardiovascular risk reduction?

CHOLESTEROL TREATMENT GOALS

With such a breadth of literature to support LDL-C as the primary target in cardiovascular risk reduction, the National Cholesterol Education Program focused on creating guidelines which utilized goals of therapy and cutpoints for medication initiation in terms of LDL-C. Initial monitoring of lipid



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Objectives

At the conclusion of this activity, pharmacists should be able to:

- Compare second-line lipid lowering agents for special patient populations
- Assess carotid artery media thickness as a clinical endpoint
- Evaluate the primary literature of ezetimibe versus niacin as a guide for therapy management of cardiovascular risk reduction

profiles, including total cholesterol, LDL, HDL and triglycerides, should begin at age 20 and at least every 5 years thereafter. Factors that increase a patient's risk for CHD, and can independently affect the LDL-C treatment goals, are listed in Table 1. The LDL-C treatment goals are stratified into three categories based on the number of independent risk factors or history of CHD or CHD equivalent.⁹ CHD risk equivalents include other clinical forms of atherosclerotic disease, such as peripheral artery disease, carotid artery disease, abdominal aortic aneurysm, diabetes or multiple factors that present a 10-year risk for CHD >20%.⁹ The LDL-C goal is tightest for this group due to the highest amount of risk for a cardiovascular event associated. The most recent update of the ATPIII guidelines in 2004 even notes optional LDL-C goals of less than 70 mg/dL for further risk reduction. If a patient has two or more independent risk factors for CHD, a Framingham risk score is calculated to determine a 10-year risk of developing CHD. This risk score not only assesses a patient's risk based on independent risk factors, but also stratifies this risk based on age, severity of current cholesterol levels and blood pressure, and cigarette smoking status.⁹ Table 2 notes the LDL-C treatment goals based on risk assessment. Obesity, physical

TABLE 1: INDEPENDENT RISK FACTORS THAT MAY MODIFY LDL-C GOALS

- Cigarette smoking
- Hypertension (BP ≥140/90 or currently treated for hypertension)
- Low HDL (<40 mg/dL)
- Family history of premature CHD (CHD in male first degree relative <55 years or female first degree relative <65 years)
- Age (male ≥45 years, female ≥55 years)

Adapted from Executive Summary of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III).⁷

TABLE 2: LDL-C CHOLESTEROL GOALS

Risk Category	LDL-C Goal (mg/dL)
0-1 Risk Factors	<160
≥2 Risk Factors or 10-yr Risk ≤20%	<130
CHD or Risk Equivalent or 10-yr Risk >20%	<100 (optional goal <70)

Adapted from Executive Summary of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III).⁷

inactivity and diet are “life-habit” risk factors that may be targets for clinical intervention; however they do not alter LDL-C goals. Emerging risk factors, including lipoprotein (a), homocysteine, impaired fasting glucose and pro-inflammatory factors, currently do not play a role in categorical changes in LDL-C treatment goals; however these factors may be used to determine those patients best suited for intensified lipid lowering therapy.

Therapy with pharmacological interventions should be initiated once LDL-C levels are 30 mg/dL greater than the prescribed LDL-C goal. Before that juncture, therapeutic lifestyle modifications are the mainstay. Dietary changes are important where saturated fat and cholesterol intake is limited in order to reduce LDL-C. Physical activity is another key component. For those patients who are obese or sedentary, moderate physical activity will enhance LDL lowering. If LDL-C goals are not met with initial dietary and increased physical activity, the addition of plant stanols or increased viscous fiber intake may be beneficial. Medicinal intervention may be warranted if these stepwise therapeutic lifestyle modifications do not bring LDL-C levels to goal.⁹ There are a variety of pharmacological options available for reaching LDL-C goals after therapeutic lifestyle changes have been exhausted.

The first-line agents for reduction in LDL-C are statins. These medications typically render a potent 20-50% lowering of LDL-C and have additional anti-inflammatory effects which compound their cardiovascular risk reductions. Statins are generally well-tolerated although clinicians must monitor for myopathy and hepatotoxicity. However, even with such extensive LDL-C lowering, statin medications do not treat all patients to their LDL-C goal and other lipid lowering agents may be required. Alternative lipid lowering agents for utilization

include bile acid sequestrants, fibric acids, ezetimibe and niacin. Bile acid sequestrants can have a large effect on LDL-C, with reductions of 15-30%, however they are poorly tolerated. With significant adverse drug effects, such as decreased absorption of other medications and undesirable gastrointestinal effects, and multiple administrations required throughout the day, adherence to this therapy is limited. Fibric acid medications can be employed for LDL-C lowering, but are more commonly utilized for reducing triglyceride (TG) levels. LDL-C reductions from fibric acid medications are typically minimal and may actually increase LDL-C in the setting of high TG. Ezetimibe and niacin have gained a niche as adjunct therapy to statin for reaching lipid goals and can lower LDL-C levels upwards of 25%.

EZETIMIBE

Ezetimibe (Zetia®) selectively inhibits cholesterol absorption in the small intestines to achieve a lipid lowering effect. It is indicated for a variety of dyslipidemias, including primary hyperlipidemia and homozygous familial hypercholesterolemia and can be used in combination with a statin or fenofibrate or as monotherapy.¹⁰ Vytorin® is the combination product of simvastatin and ezetimibe and is marketed in several dosing combinations. Patients with active liver disease, women who are pregnant or may become pregnant and nursing mothers should not use ezetimibe. Also, caution must be applied when patients have moderate or severe hepatic impairment, liver enzyme abnormalities or skeletal muscle defects due to the ability of ezetimibe to increase liver enzymes or cause rhabdomyolysis.¹⁰ The most common side effects identified with ezetimibe use are diarrhea, myalgia, arthralgia and upper respiratory tract infection. Clinically, ezetimibe reduces LDL-C levels 10-25%; however it has no effect on high density lipoprotein (HDL) or TG levels.

NIACIN

Niacin inhibits the release of free fatty acids from adipose tissue resulting in a reduced production of TG, VLDL-C, and ultimately LDL-C.¹¹ Similar to ezetimibe, niacin is indicated for primary hyperlipidemia, yet is also indicated for reduction in the risk of recurrent nonfatal myocardial infarction and treatment of severe hypertriglyceridemia.¹² Niacin is produced in multiple formulations; immediate-release (IR), sustained-release (SR) and extended-release (ER). Niaspan® is the

trade name for extended-release niacin and is only available with a prescription. Immediate-release and SR niacin formulations are available over-the-counter and are carried at most local pharmacies and health food stores.

There is a varying degree of safety with using the over-the-counter formulations. One randomized, double-blind, parallel comparison of IR and SR niacin showed increased hepatotoxicity in those patients taking ≥1500 mg of SR niacin daily (p<0.05) and increased mean fasting blood glucose in those patients taking >2000 mg of SR niacin daily (p<0.009). No significant changes in these parameters were found in the IR niacin group.¹³ There currently is a lack of evidence to link ER niacin and hepatotoxicity. Sustained-release niacin formulations should be avoided due to this increased risk of hepatotoxicity versus IR or ER niacin.¹⁴ Niacin should also not be used in patients with active peptic ulcer disease or arterial bleeding. Caution should be used when utilizing niacin for hyperlipidemia in patients with a history of myopathy, liver enzyme abnormalities, unstable angina, diabetes, gout or concomitant use of vasodilators or anti-coagulants. Common side effects associated

TABLE 3: NIACIN TITRATION STRATEGY – IR NIACIN FORMULATION

	AM	PM
Days 1 - 3	0	125 mg
Days 4 - 7	125 mg	125 mg
Days 8 - 10	125 mg	250 mg
Days 11 - 14	250 mg	250 mg
Week 3 - 4	250 mg	500 mg
Week 5 - 6	500 mg	500 mg
Week 7 - 8	500 mg	1000 mg
Week 9+	1000 mg	1000 mg

Adapted from Duke University Hospital Lipid Clinic Protocol

with niacin use include flushing, diarrhea, nausea, vomiting, hyperglycemia and hepatic dysfunction.⁹ The flushing reaction caused by niacin can be quite cumbersome, causing many patients to discontinue use before the full effects are seen. Niacin induces the release of prostaglandin D2 from Langerhans cells of the skin causing this vasocutaneous flushing response.¹¹ Slow titration of niacin is extremely important in order to for patients to build tolerance to this reaction. One dos-

TABLE 4: ARIC STUDY RESULTS

CIMT (mm)	Incidence Rates (per 1,000 person-years)	
	Women	Men
≥ 1.0	11.7	12.9
0.8 – 1.0	3.8	10.7
0.7 – 0.8	3.4	6.5
0.6 – 0.7	1.8	4.4
< 0.6	0.6	3.0

Adapted from Chambless LE, et al.¹⁷

ing titration strategy for IR niacin is noted in Table 3 (page 13). Pretreatment with aspirin 325 mg 30 minutes prior to each niacin dose can also reduce the flushing effects. Another dosing strategy for the ER niacin formulation is administering it as a bedtime dose, thus the patient will sleep through the flushing reaction. Clinically, niacin reduces LDL-C 10-25% and is the most effective agent for increasing HDL (15-35%). TG levels are also decreased 20-50%.

ENHANCE TRIAL

Since its release in 2002, ezetimibe has been widely used due to its consistent LDL-C lowering ability and limited adverse events. This trend began to change in 2008 upon the release of the Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression (ENHANCE) trial. This was a double-blind, randomized, 24-month trial comparing the effects of monotherapy simvastatin 80 mg daily versus simvastatin 80 mg daily with ezetimibe 10 mg daily on the change in mean carotid-artery intima-media thickness (CIMT). Secondary endpoints measured the proportion of patients with regression of CIMT from baseline and with new carotid-artery plaques as well as the change in the mean maximal CIMT.¹⁵ Even though the combination therapy group experienced reduced LDL-C levels of 16.5% ($p < 0.01$), there was no statistical difference in the change of CIMT from baseline between the two groups ($p = 0.29$). None of the secondary endpoints met statistical significance either.¹⁵ This lack of data for clinical improvement with ezetimibe raised questions for its continued utility. However, due to the highly specialized diagnosis being treated, familial hypercholesterolemia, the generalizability of this data is limited and continued use of ezetimibe has occurred. The National Lipid Association and the American Heart Association, in conjunction with the American College of Cardiology,

took the release of this data as an opportunity to reinforce the current guidelines. All three organizations emphasized that the evidence for cardiovascular risk reduction supported statin utilization first, then bile acid sequestrants and niacin before consideration of ezetimibe for treatment.

CAROTID-ARTERY INTIMA MEDIA THICKNESS (CIMT)

Unlike other large cardiology studies, the ENHANCE trial chose to use CIMT as the primary endpoint in place of adverse cardiovascular events or all-cause mortality. CIMT is a measurement by B-mode ultrasound of the thickness of the intima and media level of the carotid artery. The logic of this measurement stems from a histologic relation seen in autopsy studies between carotid and coronary atherosclerosis. Generally speaking, if there is atherosclerosis in the coronary arteries, it is likely to be present (and measurable) elsewhere as well.

CIMT measurements require a high level of precision and accuracy as they are measured to the level of a hundredth, and occasionally a thousandth, of a millimeter. Additionally, measurements need to be taken in accordance with EKG gating to assist in the selection of images from specific sequences within the cardiac cycle. This makes reproducibility difficult for novice technicians. Use of a skilled ultrasonographer and quality control protocols are extremely important in trials which utilize this endpoint in order to reduce measurement variability and to increase the power of a study. An absolute definition of a clinically significant CIMT is problematic due to the strong influence of age and gender on arterial wall thickness. Use of an absolute threshold to define an abnormal value, similar to other laboratory values, may result in underestimation in younger patients and overestimation in older patients. Thus, population databases are imperative to properly interpret CIMT values.¹⁶

One of the first trials to evaluate CIMT measurement was the Atherosclerosis Risk in Communities (ARIC) study. This study included 12,841 men and women aged 45-64 years who were free of CHD at baseline. Their CIMT was measured at baseline and again in 5 years and compared for correlation. There was a clear increase in CHD events as CIMT increased (Table 4).¹⁷ The Cardiovascular Health Study was a multicenter study of similar design to ARIC that followed patients for approximately 6 years with an endpoint of

myocardial infarction and stroke. Their results also demonstrated a clear increase in events with increased CIMT. The investigators also looked at the relative risk after adjustment for established risk factors, including blood pressure, diabetes, smoking, and atrial fibrillation. When adjusted for age and sex, the relative risk was 1.44 (versus 1.58 unadjusted risk). When adjusted for age, sex and the above risk factors, the relative risk was 1.36. Both adjustments retained statistical significance.¹⁸

Multiple trials have evaluated the effect of lipid lowering therapy on CIMT progression. A substudy of the REGRESS trial evaluated the effect of pravastatin 40 mg daily versus placebo over 2 years. Mean CIMT decreased 0.05 mm in the pravastatin group but remained unchanged in the placebo group.¹⁹ The ARBITER trial

TABLE 5: PERCENT CHANGES IN CHOLESTEROL FROM BASELINE AT 14 MONTHS

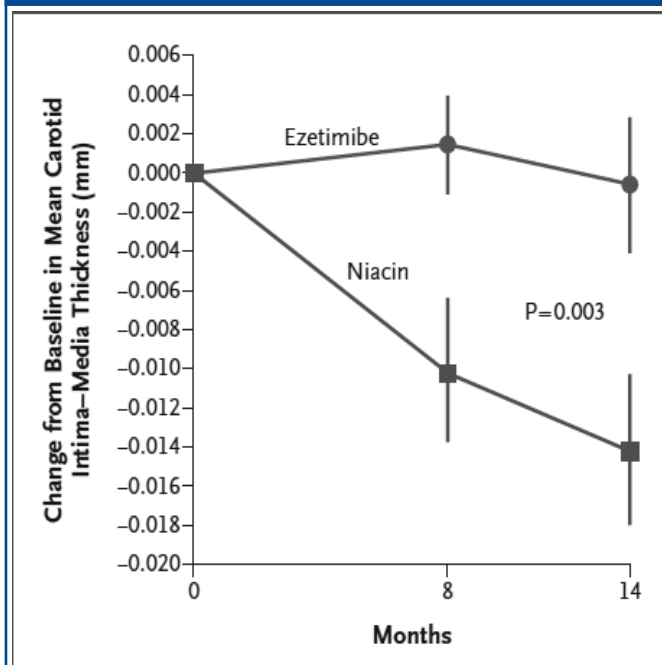
	Statin + Ezetimibe	Statin + ER Niacin
Total Cholesterol	↓ 13%	↓ 8%
LDL-C	↓ 18%	↓ 10%
HDL	↓ 3%	↑ 8%
Triglycerides	↑ 1%	↓ 16%

Adapted from Taylor, et al.¹⁵

was an active control trial of patients who qualified for lipid lowering therapy based on ATP criteria.²⁰ Patients were randomized to pravastatin 40 mg daily or atorvastatin 80 mg daily with a 12-month follow up. CIMT measurements decreased in the atorvastatin group but remained stable in the pravastatin group.²⁰ Trials such as these demonstrate that CIMT progression can be halted, and even reversed, with intensive lipid lowering therapy.

These trials used change in CIMT as their primary outcome; however patients were not usually followed for event rates. The CLAS follow-up study specifically aimed to look at events with a purpose to determine whether change in CIMT predicts cardiovascular events. Patients were treated with colestipol and niacin for 2 years and then followed an additional 8.8 years. For each 0.03 mm increase in CIMT, the relative risk for MI or cardiovascular death was 2.2 and for coronary events 3.1. These findings were independent of any changes seen through angiography.²¹ Although this was a small study, it did link CIMT progression as an independent predictor of hard clinical outcomes. These trials

FIGURE 1: PRIMARY ENDPOINT RESULTS



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have validated the use of CIMT measurement as a surrogate marker of cardiovascular risk.

A key advantage for any surrogate marker is that its use can enable the detection of statistically significant differences between therapeutic regimens with substantially smaller sample sizes and within a shorter period of time. CIMT studies generally only require several hundred subjects followed for 12 to 24 months which is very appealing for pharmaceutical intervention research. The safety profile of CIMT is also quite favorable as this test is non-invasive, does not expose patients to radiation, and has no known biological adverse effects. It is widely available and takes approximately 45-60 minutes to complete.¹⁶

Limitations are inherent and CIMT is not impervious from these obstacles. Besides the technical difficulties already discussed, there is a lack of data in younger patients. Thus, CIMT measurement is generally not recommended in patients younger than 45 years old. Additionally, CIMT does have an ICD-9 code for third party billing, however many third parties do not cover this test, so patients must pay out-of-pocket. A CIMT measurement generally costs between \$400 and \$500. This financial hindrance has limited CIMT use as a clinical marker outside of the investigational realm.

Overall, CIMT is a useful tool as a predictor for future CHD events as well

hypercholesterolemia. The Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL-C Treatment Strategies (ARBITER-6 HALTS) trial sought to compare the effects of either ezetimibe or niacin added to long-term statin therapy on CIMT over a 14-month period.²² This was a randomized, parallel group, open label study that included patients 30 years of age or older who had either known atherosclerotic

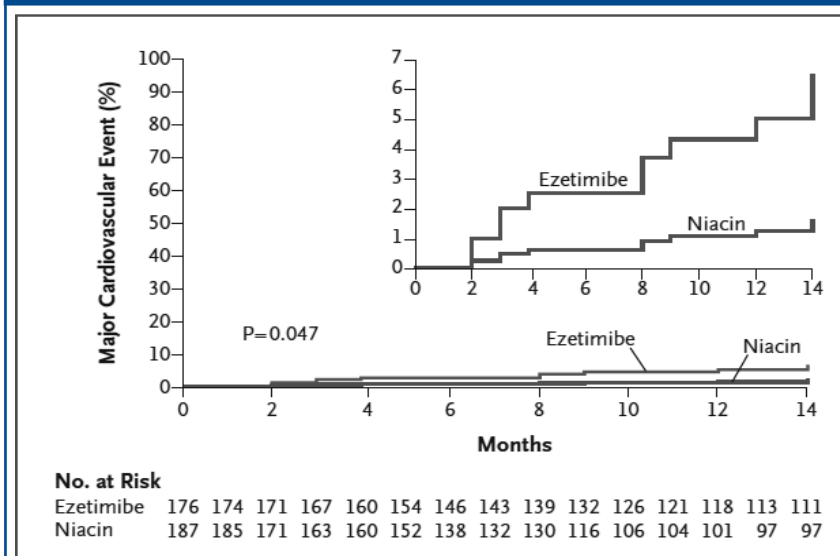
as current coronary artery disease status. It is a measurement that will continue to be used in clinical trials and may someday find its way into general practice. It is important for pharmacists to have a basic understanding of the technique and interpretation.

ARBITER-6 HALTS TRIAL

After the ENHANCE trial failed to show clinical value of the addition of ezetimibe to simvastatin therapy, further research was necessary to outline the clinical use and efficacy of ezetimibe as adjunct therapy for

coronary or vascular disease or a coronary heart disease risk equivalent, including diabetes mellitus, a 10-year Framingham risk score of 20% or more or a coronary calcium score above 200 for women or 400 for men. Prior to enrollment, patients were relatively well controlled on statin therapy with LDL-C levels <100 mg/dL but HDL levels <50 mg/dL for men and <55 mg/dL for women. Patients were continued on their previous statin therapy and randomized to either ezetimibe 10 mg daily or ER niacin 500 mg at bedtime and titrated every other week by 500 mg to 2000 mg or the maximum tolerated dose. The primary end point was the between-group difference in the change in mean carotid intima-media thickness after 14 months. Secondary end points identified the change in lipid values from baseline, a composite end point consisting of major adverse cardiovascular events (including myocardial infarction, myocardial revascularization, admission to the hospital for an acute coronary syndrome, and death from coronary heart disease), discontinuation of a study drug owing to adverse effects, and health-related quality of life.²² An independent data advisory committee unanimously recommended early termination of the study due to preliminary results; thus the study only reached inclusion of 208 patients, 92 patients short of meeting 80% statistical power. Patient demographics were similar in both treatment groups, with the majority of the patients being approximately 65 year old males treated with either atorvastatin or simvastatin. The only

FIGURE 2: PERCENTAGE OF MAJOR CARDIOVASCULAR EVENTS



No. at Risk

Ezetimibe	176	174	171	167	160	154	146	143	139	132	126	121	118	113	111
Niacin	187	185	171	163	160	152	138	132	130	116	106	104	101	97	97

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statistical difference between the two groups was the increased number of patients in the ezetimibe arm who underwent percutaneous coronary revascularization. Reductions in cholesterol levels were as expected in the two groups, as noted in Table 5. Ezetimibe only rendered decreases in total cholesterol and LDL-C, while niacin provided decreases for total cholesterol, LDL-C and TGs and increased HDL-C levels. Figure 1 depicts the primary endpoint showing statistical difference in change from baseline CIMT between niacin and ezetimibe groups ($p=0.003$).²² Major adverse cardiovascular events occurred

positive clinical outcomes and hinges on the reduction of LDL-C levels. Statin medications will continue to be the cornerstone therapy for primary reduction in risk and LDL-C. However, when a patient is not reaching his/her lipid goals, niacin appears to be the better choice based on current evidence. With the most recent paradoxical findings of ezetimibe and increases in CIMT, clinical use of this agent should be done with caution and utilized only when other options have been exhausted. The Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE IT) is a randomized,

With the most recent paradoxical findings of ezetimibe and increases in CIMT, clinical use of this agent should be done with caution and utilized only when other options have been exhausted.

more frequently in the ezetimibe versus niacin group ($p=0.04$, Figure 2), however this was a secondary endpoint. In post hoc analysis, an inverse relationship was identified in the ezetimibe group, noting increased CIMT in those patients with larger decreases in LDL-C levels ($p<0.001$).²²

The ARBITER-6 HALTS study concluded ER niacin causes a significant regression of CIMT when combined with a statin over ezetimibe. Extended-release niacin administration not only led to a larger regression of CIMT, but also resulted in fewer major cardiovascular events than ezetimibe.²² More concerning was the paradoxical relationship of ezetimibe on increased cardiovascular risk, specifically atherosclerotic progression. Further research is needed to fully understand the safety implications the ARBITER-6 HALTS study raised with ezetimibe use. Limitations from this study include the open label design, where patient bias can confound results. The reduced sample size also hinders the power of this research and hence the generalizability of this study to larger populations.

CLINICAL CONCLUSION

Cardiovascular risk reduction for those with hypercholesterolemia is important for

active-control, double-blind study currently underway which seeks to evaluate the clinical benefit of ezetimibe in combination with simvastatin on cardiovascular endpoints, including death, major cardiovascular events and stroke.¹⁸ This trial, that is scheduled to be completed in mid-2013, will help guide the recommendation for utilization of ezetimibe for cardiovascular risk reduction and lipid-lowering. ●

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ASSESSMENT QUESTIONS

Ezetimibe vs Niacin



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NC is a 58 yo Caucasian male with hypertension, transient ischemic attacks, hyperlipidemia and allergic rhinitis. He does not smoke and reports drinking one glass of red wine with dinner each night. His most recent pertinent lab results are as follows: TC = 209 mg/dL, LDL = 103 mg/dL, HDL = 41 mg/dL, TG = 325 mg/dL, and glucose 105 mg/dL. Vitals today are: BP 140/90 mmHg and pulse 80 bpm. His weight is 120 kg and his waistline is measured at 44 in. Current medications include clopidogrel 75 mg PO daily, cetirizine 10 mg PO daily, lisinopril 20 mg PO daily, and simvastatin 40 mg PO qhs.

- Which of the following is the most accurate list of NC's LDL-modifying risk factors based on the information given?
 - Age, hypertension, carotid artery disease
 - Age, alcohol use, hypertension
 - Age, waist circumference, carotid artery disease, hypertension
 - Age, hypertension
 - During your review of NC's past medical history, you realize that he has a CHD risk equivalent. Which of the following is considered a risk equivalent?
 - Hypertension
 - Carotid artery disease
 - Peripheral artery disease
 - Obesity
 - What is NC's LDL goal?
 - Less than 70 mg/dL
 - Less than 100 mg/dL
 - Less than 100 mg/dL with an optional goal of less than 70 mg/dL
 - Less than 130 mg/dL with an optional goal of less than 100 mg/dL
 - Which of the following is true regarding appropriate counseling prior to initiation of niacin therapy?
 - Niacin and statins should not be used in combination due to increased risk of myopathy
 - Niacin should be taken on an empty stomach
 - Flushing is minimized by taking the total daily dose all at once
 - Slow dose titration is extremely important to minimize side effects
 - Which of the following medications is the most effective for raising HDL?
 - Atorvastatin
 - Niacin
 - Fenofibrate
 - Colesevelam
 - Which of the following is true regarding adverse drug reactions of bile acid resins?
 - The risk of hepatotoxicity is >10%
 - The risk of myopathy is <5%
 - Bile acid resins are generally not tolerated well due to GI intolerance
 - Bile acid resins are generally not tolerated well due to the adverse effect of flushing
- JC is a 48 yo male with a PMH of diabetes, GERD and hypothyroidism. JC does not smoke or drink alcohol. Vitals today are: BP 128/85 mmHg and pulse 70 bpm. His weight is 115 kg and his waistline is measured at 40 in. Current medications include omeprazole 20 mg PO daily, aspirin 81 mg PO daily, levothyroxine 125 mcg PO daily and metformin 500 mg PO BID. His lipid panel is reported as: TC 217 mg/dL, LDL 130 mg/dL, HDL 36 mg/dL, TG 255 mg/dL.
- Which of the following is the best medication choice for JC?
 - Simvastatin 20 mg PO qhs
 - Ezetimibe 10 mg PO daily
 - Colesevelam 625 mg, titrate to 7 tablets daily
 - Gemfibrozil 600 mg PO BID
- LH is a 50 yo African American female with a past medical history significant for hyperlipidemia and asthma. Both of her parents have established coronary artery disease (father experienced a nonfatal myocardial infarction at 49 years of age). LH smokes ½ ppd. She does not drink and she exercises 3 days/week. Her current medications include atorvastatin 20 mg PO qhs, Advair Diskus 250/50 one INH BID, and albuterol 2 puffs q4h prn (she has been on this regimen for about 2 years). Current lab results include TC = 225 mg/dL, LDL = 156 mg/dL, HDL = 34 mg/dL, TG = 175 mg/dL, AST = 34 units/L, and ALT = 25 units/L.
- How many CHD risk factors does LH have?
 - Three – age, hyperlipidemia and family history
 - Three – smoking status, family history and low HDL
 - Two – hyperlipidemia and family history
 - Two – age and low HDL
 - Because LH has (a minimum of) 2 risk factors, you conduct a Framingham risk assessment and calculate a 10-year CHD risk of <10%. What LDL goal do you set for LH?
 - Less than 100 mg/dL
 - Less than 130 mg/dL
 - Less than 160 mg/dL
 - Less than 190 mg/dL
- You decide to intensify LH's lipid regimen – which of the following is the most reasonable choice based on evidence-based medicine and efficacy?
 - Discontinue atorvastatin and initiate IR niacin (with titration schedule)
 - Continue atorvastatin and initiate IR niacin (with titration schedule)
 - Continue atorvastatin and initiate ezetimibe 10 mg daily
 - Continue atorvastatin and initiate gemfibrozil 600 mg BID
 - Do nothing, LH's cholesterol panel is appropriate
- CIMT is clinically validated as a primary endpoint that can predict major cardiovascular events.
 - True
 - False
- The ENHANCE trial concluded:
 - There was no difference in the change in CIMT from baseline between the two groups.
 - There was no difference in cardiovascular outcomes between the two groups.
 - There was a statistical difference in the change in CIMT from baseline between the two groups.
 - There was a statistical difference in cardiovascular outcomes between the two groups.
- Which trial caused the American Heart Association and the National Lipid Association to release a statement reinforcing current guidelines for medication selection in hyperlipidemia?
 - ARBITER
 - ARIC
 - ENHANCE
 - ARBITER-6 HALTS
 - PROVE-IT
- All of the following characterize ezetimibe therapy, except:
 - The most common dose is 10 mg daily.
 - The clinical profile of ezetimibe only includes reductions in LDL.
 - Ezetimibe is only indicated as a combination therapy.
 - Ezetimibe can cause myalgias.
 - None of the above.

- 15. The ARBITER-6 HALTS trial only included patients who had either known atherosclerotic coronary or vascular disease or a coronary heart disease risk equivalent.
 - A. True
 - B. False
- 16. This activity met my educational needs
 - A. Met all educational needs related to the topic
 - B. Met some educational needs, but not all
 - C. Did not meet my needs

Did the activity meet the following stated learning objectives?

- 17. Compare second-line lipid lowering agents for special patient populations
 - A. Yes
 - B. No

- 18. Assess carotid artery media thickness as a clinical endpoint
 - A. Yes
 - B. No
- 19. Evaluate the primary literature of ezetimibe versus niacin as a guide for therapy management of cardiovascular risk reduction
 - A. Yes
 - B. No
- 20. How would you rate the ability of the author to provide a high-quality educational activity?
 - A. Very capable, article was well written and provided good information
 - B. Somewhat capable, most information was presented well
 - C. Needs improvement

- 21. How useful was this educational activity?
 - A. Very useful
 - B. Somewhat useful
 - C. Not useful
- 22. How effective were the learning methods used for this activity?
 - A. Very effective
 - B. Somewhat effective
 - C. Not effective
- 23. Learning assessment questions were appropriate
 - A. Yes
 - B. No
- 24. Was the author free of bias?
 - A. Yes
 - B. No

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- 1) a b c d
- 2) a b c d
- 3) a b c d
- 4) a b c d
- 5) a b c d
- 6) a b c d
- 7) a b c d
- 8) a b c d
- 9) a b c d
- 10) a b c d e
- 11) a b
- 12) a b c d
- 13) a b c d e
- 14) a b c d e
- 15) a b
- 16) a b c
- 17) a b
- 18) a b
- 19) a b
- 20) a b c
- 21) a b c
- 22) a b c
- 23) a b
- 24) a b

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July/August 2010

How Thick is too Thick for Your Arteries? Ezetimibe versus Niacin for Cardiovascular Risk Reduction

ACPE Universal Activity Number: 0175-0000-10-033-H01-P Target Audience: **Pharmacists**

Activity Type: **knowledge-based**

Release Date: July 1, 2010 (No longer valid for CE credit after July 1, 2013)