Seminar & Journal Club II
Seminar Outline Template

Section letter: 4

Team members: Julia Freemire, Sarah LaPaglia, Julia Wing

Instructions: Each team will complete the following outline and references sections by replacing all **RED** bracketed directives with relevant information pertaining to their seminar presentation. No **RED** bracketed sections of the outline or references should be left blank or omitted unless intended to be used for additional information, as defined.

Each CAPITALIZED heading on the Seminar Outline Template corresponds, in general, to one slide on the Seminar Presentation Template. Exceptions to this rule may include any slide that must be expanded to incorporate additional relevant information, particularly slides related to the description and evaluation of primary literature articles. Although additional outline headings (or slides) may be added to fully explain aspects relevant to the seminar or fit information onto a slide (using a minimum PowerPoint font size of 18), teams should ensure that the data they include in this outline will not force their presentations over the 30 minute time limit.

At least six (6) references should be used in the development of the seminar including, but not limited to: one (1) guideline; one (1) tertiary resource for disease state data; one (1) drug compendia for pharmacotherapy data; and three (3) primary literature articles for evaluation (with the exception of meta-analyses and expert opinions).

After completing the Seminar Outline Template, each team should incorporate the information from the outline into the corresponding slides of the Seminar Presentation Template. Both the completed Seminar Outline Template and Seminar Presentation Template should be submitted via email to Dr. Hutcherson as described in the syllabus.

Outline

1. WORKING TITLE
    a. Dyslipidemia-The Efficacy of Statin Monotherapy versus Statin and Ezetimibe Combination Therapy
2. LEARNING OBJECTIVES
    a. Analyze the guideline for dyslipidemia and be able to apply it to practice
    b. Understand dyslipidemia pathophysiology and its impact globally as well as its long term complications

c. Identify patients with dyslipidemia based on the pathophysiology and clinical presentation
d. Evaluate the medication therapy options and recommend a medication based on the dosing regimen and dosage alterations
e. Analyze and discuss literature regarding dyslipidemia medication management
f. Apply the recommendation to treat a patient with dyslipidemia

3. INTRODUCTION
    a. We will specifically be focusing on the addition of ezetimibe therapy to statin therapy to achieve a greater reduction in LDL-C levels.
    b. OUTLINE (leave outline below unchanged)
        i. Guideline overview
        ii. Disease state overview
        iii. Current therapies
        iv. Literature review
        v. Recommendation
        vi. Presentation summary
        vii. Forum for questions
4. GUIDELINE OVERVIEW
    a. This section will highlight the guideline that we will be focusing on for the management of dyslipidemia.
    b. GUIDELINE REVIEW
        i. Grundy S, Stone N, Bailey A, 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. Journal of the American College of Cardiology, 73(24), e285-e350.
        ii. The authors consist of medical experts including cardiologists, internists, interventionalists, nurse practitioners, pharmacists, physician assistants, and a patient representative.
        iii. The disease state highlighted in this guideline is dyslipidemia and the guideline focuses on the management of cholesterol utilizing non-pharmacologic treatment options as well as pharmacologic treatment options.
    c. SELECTED RECOMMENDATION
        i. “In patients with clinical ASCVD who are receiving maximally tolerated statin therapy and whose LDL-C level remains 70 mg/dL or higher (> 1.8 mmol/L), it may be reasonable to add ezetimibe.” Evidence level: B
    d. QUALITY OF EVIDENCE
        i. The recommendation chosen is a class IIa level B-R recommendation. The guideline has classes of recommendation which demonstrate the strength of the recommendation with Class I being the highest and Class III being the weakest with no benefit or potential harm. The recommendation we have chosen is a moderate recommendation with the benefit outweighing the risk. The second systematic method the guideline uses to organize the recommendations is the level of evidence also known as quality, with A being the best quality and C-EO being the lowest. Level B-R is randomized, moderate quality evidence.
5. DISEASE STATE OVERVIEW

a. Dyslipidemia is an imbalance of lipids in the blood and it often involves a high level of cholesterol or triglycerides. It impacts a large proportion of the population and has numerous therapies to aid in the management of high cholesterol.
b. EPIDEMIOLOGY
    i. In the United States, 15% of adults have total serum cholesterol leve;s of 240 mg/dL or higher, 69% have LDL-C levels over 100 mg/dL, and 33% have elevated triglyceride levels.
    ii. In the United States, approximately 33,600,000 adults 20 years or older have total serum cholesterol levels of 240 mg/dL or higher.
    iii. Raised cholesterol levels increase the risk of other cardiovascular diseases, such as heart disease and stroke. Globally, a third of ischaemic heart disease is attributable to high cholesterol; therefore, raised cholesterol is estimated to cause 2.6 million deaths.
c. ETIOLOGY
    i. Dyslipidemia may be acquired or familial; however, in most individuals, dyslipidemia is associated with lifestyle factors or liver and renal diseases. In some patients, an underlying factor is responsible for the development of dyslipidemia, through either overproduction or decreased clearance of triglycerides or low density lipoprotein or an underproduction or increased clearance of high density lipoprotein cholesterol.
    ii. Numerous factors can contribute to the development of dyslipidemia, including medications, diet, smoking, inactivity, endocrine disorders, liver or renal diseases, or it is familial.
d. PATHOPHYSIOLOGY
    i. Atherosclerosis is the formation of plaque from a buildup of fats, cholesterol, and other substances on the inner walls of the arteries. Lipoproteins are the root cause as they migrate between the endothelial cells into the arterial wall where they are oxidized. There are two ways in which an increase in lipids can happen: primary, or familial, and secondary, or acquired. In primary dyslipidemia, genetic defects can cause severe cholesterol elevations. In secondary dyslipidemia, years of poor diet, sedentary lifestyle and lifestyle factors cause central adiposity.
    ii. The physiological markers of the disease are high LDL levels (190+ mg/dL) and high triglyceride levels (500+ mg/dL). In cases of severely elevated triglycerides specifically, over 1000 mg/dL, patients may present with pancreatitis.
    iii. The disease progresses from high cholesterol, to the buildup of plaque in arteries ultimately leading to numerous complications, including acute myocardial infarction, heart failure, coronary arteriosclerosis, thromboembolic stroke, peripheral vascular disease, and pancreatitis.

6. CURRENT THERAPIES
    a. This section will highlight the current therapies that are utilized for the management of dyslipidemia and the progression of dyslipidemia to further complications.
    b. GOALS OF THERAPY
        i. The primary goal of pharmacotherapy for dyslipidemia is to lower LDL-C levels and triglycerides to a desirable level of < 100 mg/dL and <150 mg/dL respectively.
    c. CURRENT TREATMENT OPTIONS
        i. As it relates to the recommendation, the current treatment options would include:

1. Statin Therapy Options
    a. Atorvastatin (Brand name: Lipitor)
    b. Rosuvastatin (Brand name: Crestor)
    c. Simvastatin (Brand name: Zocor)
    d. Pravastatin (Brand name: Pravachol)
    e. Lovastatin (Brand name: Altoprev)
    f. Fluvastatin (Brand name: Lescol)
    g. Pitavastatin (Brand name: Livalo)
    h. MOA: Statins are selective, competitive inhibitors of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. This is a rate limiting enzyme that is responsible for converting HMG-CoA to mevalonate, which is a precursor to sterols (cholesterol). By inhibiting HMG-CoA reductase, this lowers the amount of mevalonate produced and will therefore lower cholesterol levels. In turn, this allows for an upregulation of LDL-receptors and increased uptake of LDL from the circulation.
2. Ezetimibe (Brand name: Zetia)
    a. MOA: Ezetimibe works to lower cholesterol by selectively inhibiting the absorption of cholesterol. The mechanism of action complements that of an HMG-CoA reductase inhibitor and results in synergistic cholesterol-lowering effects. The molecular target of ezetimibe is the Niemann-Pick C1-Like 1 (NPC1L1) transporter by inhibiting the uptake of cholesterol which decreases the delivery of cholesterol to the liver. This will then lead to a decrease in hepatic cholesterol stores and an increase in blood clearance of cholesterol.

d. GUIDELINE-SPECIFIC THERAPIES
    i. The 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease recommends that patients are initiated on statin therapy and add-on therapies, such as ezetimibe, are introduced as needed. Before the addition of ezetimibe, patients should be counseled on the importance of medication adherence and to incorporate lifestyle changes.
e. PHARMACOLOGY/ DOSING
    i. Statins are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme of cholesterol synthesis. Ezetimibe inhibits the absorption of cholesterol at the brush border of the small intestine via the sterol transporter, thus leading to a decreased delivery of cholesterol to the liver, reduction of hepatic cholesterol stores and an increased clearance of cholesterol from the blood.
    ii. Rosuvastatin:
        1. Rosuvastatin is considered to be a high intensity statin and a moderate intensity statin based on the dose. Rosuvastatin is a high intensity statin at doses of 20 mg and 40 mg and a moderate intensity statin at doses 5 mg and 10 mg. It is taken by mouth once daily and has a maximum dose of 40 mg/ day. It requires very little dose adjustments, except when CrCl is less than 30 mL/min/1.73m^2, there is a maximum dose of 5-10 mg once daily. When a patient is undergoing hemodialysis, there is a maximum dose of 10 mg/day.

iii. Atorvastatin:
1. Atorvastatin is also considered to be a high intensity statin and a moderate intensity based on the dose. Atorvastatin is a high intensity statin at doses 40 mg and 80 mg and a moderate intensity statin 5 mg and 10 mg. It is taken by mouth once daily and has a maximum dose of 80 mg/day. It does not require any dose adjustments.

iv. Ezetimibe
1. Ezetimibe is an add on therapy in dyslipidemia and is 10 mg taken by mouth once daily. As this medication is only available in 10 mg formulation, it has a max daily dose of 10 mg/day. There are no dosage adjustments required; however, its use in moderate to severe hepatic impairment is not recommended.

f. ADVERSE EVENTS
i. Rosuvastatin:
1. constipation, nausea, dizziness, headache, arthralgia, abdominal pain

ii. Atorvastatin:
1. diarrhea, arthralgia, dyspepsia, nausea, urinary tract infection

iii. Ezetimibe:
1. arthralgia, upper respiratory tract infection, skin rash, abdominal pain

7. LITERATURE REVIEW
a. This section will review the studies evaluating the efficacy of statin monotherapy versus statin therapy plus add on ezetimibe therapy.
b. LITERATURE SEARCH
i. The three articles used in this seminar were found using bibliographic sources found in the dyslipidemia guideline that directly compare the effects of statin monotherapy versus combination therapy with a statin and ezetimibe.
c. SELECTED ARTICLES FOR EVALUATION
i. The following three articles will be evaluated in the recommendation of ezetimibe add-on therapy in the management of dyslipidemia.
ii. Article 1: Lee *et al*
1. randomized controlled trial– superiority study

iii. Article 2: Catapano *et al*
1. randomized controlled trial– superiority study

iv. Article 3: Bays *et al*
1. randomized controlled trial– superiority study

v. [brief yet logical segue to first article/presenter, if applicable]

8. ARTICLE 1:
a. Lee S, Kim W, Jong Hong T, *et al*. Effects of fixed-dose combination of low-intensity rosuvastatin and ezetimibe versus moderate-intensity rosuvastatin monotherapy on lipid profiles in patients with hypercholesterolemia: A randomized double-blind, multicenter phase III study.
b. Lee *et al*
i. randomized controlled trial–superiority study
ii. Korea
iii. Multi-centered study
iv. The objective of this study was to investigate the combination therapy of low-intensity rosuvastatin and ezetimibe as a useful alternative to

moderate-intensity rosuvastatin monotherapy in patients requiring cholesterol-lowering therapy.

v. The primary efficacy endpoint in this study was the percent change in LDL-C levels at the 8 week follow-up.
vi. In this study, there were 4 treatment groups; 2.5/10 mg of rosuvastatin and ezetimibe, 10 mg of ezetimibe, 2.5 mg of rosuvastatin, and 5 mg of rosuvastatin.
vii. Patients were over 19 years old, had fasting serum levels of LDL-C greater than or equal to 250 mg/dL and triglyceride levels greater than equal to 500 mg/dL.
viii. Exclusion criteria included patients with coronary artery syndrome, advanced heart failure, history of percutaneous coronary intervention or coronary bypass graft surgery.
ix. The study lasted 8 weeks.
x. Participants were randomly assigned in a 1:1:1:1 ratio to four groups using a Web-based interactive response system.
    1. The randomization led to similar groups.
xi. Data Analysis
    1. Intent to Treat
    2. <0.05
    3. 98%
    4. 240
    5. 279
    6. Power was met
    7. Percent change in LDL-C levels at the 8 week follow-up
    8. Interval/ratio data
    9. Wilcoxon rank-sum tests
    10. The statistical test was appropriate for the data
xii. The target achievements were significantly higher in the combination therapy group than in the ezetimibe 10 mg group, with a $p< 0.0001$ as well as both of the rosuvastatin monotherapy groups with 2.5 mg and 5 mg with p-values of $p< 0.0001$ and $p= 0.0092$ respectively. The percentage of patients achieving LDL levels <70 mg/dL or a reduction of LDL greater than or equal to 50% was significantly higher in the combination therapy group than other groups, with a $p< 0.001$.
xiii. Adverse events occurred in 7 patients, 2.5%, and there were no differences in adverse effects between the treatment groups. Most adverse events were mild and the most common adverse effects were dyspepsia and pruritus.
xiv. The authors concluded that combination therapy with low intensity rosuvastatin and ezetimibe resulted in a greater reduction in LDL-C than moderate intensity rosuvastatin monotherapy and has more benefits to the patient.
xv. Power was set and met, the biostatistical test was appropriate for the data type, the outcome measure is accepted practice, inclusion and exclusion criteria are adequate, randomization resulted in similar groups, the length of the study was appropriate to show effect, the treatment regimen is appropriate, the blinding was sufficient to mask data, and the authors conclusion was supported by the results.
xvi. This study only involved an Asian population, therefore extrapolation of these data to other ethnic groups may be limited.
xvii. This is a level I study with minor limitations

c. [brief yet logical segue to next article/presenter, if applicable]

9. ARTICLE 2:
    a. Catapano A, Vrablik M, Karpov Y, *et al*. A Phase 3 Randomized Controlled Trial to Evaluate Efficacy and Safety of New-Formulation Zenon (Rosuvastatin/Ezetimibe Fixed-Dose Combination) in Primary Hypercholesterolemia Inadequately Controlled by Statins. J Cardio Pharm Ther. 2022; 27 (1): 107-111.
    b. Catapano *et al*
        i. Randomized controlled trial– superiority study
        ii. Bulgaria, Czech Republic, Italy, Mexico, Poland, Russia, Slovakia, and Ukraine
        iii. multi-centered
        iv. The objective of this study was to evaluate the efficacy and safety of a new fixed-dose combination of rosuvastatin/ ezetimibe in a population of patients who did not reach their LDL-C goals and are at an increased risk of cardiovascular disease.
        v. The primary efficacy endpoint was a change from baseline in calculated LDL-C at week 6.
        vi. In this study, there were 3 treatment arms, each receiving a different dose of medication and combination: rosuvastatin 20 mg/ ezetimibe 10 mg, rosuvastatin 40 mg/ ezetimibe 10 mg, or rosuvastatin 40 mg.
        vii. Inclusion criteria included hypercholesterolemia not adequately controlled.
        viii. Patients were excluded from the study if they had homozygous familial hypercholesterolemia, unstable angina, myocardial revascularization, coronary artery bypass graft surgery, stroke, or surgical intervention for peripheral vascular disease.
        ix. The study lasted 16 weeks.
        x. Randomization was performed using VHR and HR strata using an interactive response technology to allocate numbered treatment kits and was stratified by country.
            1. Randomization led to similar groups.
        xi. Data Analysis
            1. modified intent to treat
            2. 0.05
            3. 97%
            4. 355
            5. 452
            6. Power was set and met
            7. The primary efficacy measure was a change from baseline in calculated LDL-C at week 6.
            8. Ordinal data
            9. ANCOVA
            10. The statistical test is appropriate for the data.
        xii. The superiority of the combination medications R40/E10 and R20/E10 over R40 was demonstrated with LS mean differences of LDL-C percent change -19.66% and -12.28% with p-values of $p<0.001$ and $p=0.015$, respectively.
        xiii. No unexpected safety findings were reported during the study, with reports of mainly gastrointestinal side effects, such as dyspepsia. No clinically meaningful abnormalities in laboratory assessments or vital signs were observed.

xiv. The authors concluded that a combination medication formulation of rosuvastatin and ezetimibe improve LDL-C reduction and enable more patients to reach LDL-C targets compared with rosuvastatin monotherapy.
xv. Power was set and met, biostatistical test was appropriate for the data type, the outcome measure is valid or accepted practice, inclusion and exclusion criteria are adequate, randomization resulted in similar groups, the length of the study was appropriate to show effect, the treatment regimen is appropriate, blinding is sufficient to mask data, the authors conclusions are supported by the results.
xvi. Further research is required to determine the full uses and effects of these combination therapies in treatment regimens.
xvii. Level I study with minor limitations

c. [brief yet logical segue to next article/presenter, if applicable]

10. ARTICLE 3:
    a. Bays HE, Averna M, Majul C, et al. Efficacy and safety of ezetimibe added to atorvastatin versus atorvastatin uptitration or switching to rosuvastatin in patients with primary hypercholesterolemia. American Journal of Cardiology. 2013; 112: 1885-1895.
    b. Bays *et al*
        i. randomized controlled trial – superiority study
        ii. Argentina, Belgium, Bulgaria, Canada, Chile, Columbia, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Israel , Italy, Lithuania , the Netherlands , Norway, Poland, Portugal , Romania, Slovakia, Slovenia , Spain , Sweden , Turkey, the United Kingdom, and the United States
        iii. Multi-centered study
        iv. The object of the study is to evaluate the efficacy and safety of Ezetimibe Added to Atorvastatin Versus Atorvastatin Uptitration or Switching to Rosuvastatin in Patients With Primary Hypercholesterolemia and its effect on lowering LDL-C.
        v. The primary efficacy endpoint variable was the percent change from treated baseline in LDL-C levels at the end of period I. Secondary end point variables included percent change from treated baseline in LDL-C at the end of period II; percentage of subjects achieving LDL-C <100 or <70 mg/dl at the end of periods I and II; percent change from treated baseline in other lipids, lipoproteins, and high sensitivity C-reactive protein (hs-CRP) at the end of periods I and II; assessment of safety and tolerability.
        vi. An anticipated number of patients not adequately controlled on atorvastatin 20 mg/day (50%) or rosuvastatin 10 mg/day (40%) after period I.
        vii. Men and women of nonchildbearing potential and aged 18 and <80 years with primary hypercholesterolemia. Subjects were required to be at high CVD risk and meet prespecified lipid entry criteria. The high CVD risk study entry criteria included subjects without CVD who had type 2 diabetes mellitus or 2 CVD risk factors and a 10-year risk for coronary heart disease >20%.
        viii. Main exclusion criteria included alanine aminotransferase or aspartate aminotransferase levels >2 the upper limit of normal; creatine kinase >3 , a history of significant myopathy or rhabdomyolysis with any statin or ezetimibe; hypersensitivity or intolerance to ezetimibe, atorvastatin, rosuvastatin, or any component of these medications; congestive heart failure.
        ix. two 6-week study period- period I & II
        x. randomization led to similar groups
        xi. Data analysis

1. ITT
2. 0.001
3. 0.05 and 90%
4. 1500
5. 1547
6. Power was set and met
7. The primary efficacy measure was a change from baseline in calculated LDL-C at week 6 for period I and LDL-C at week 12 for period ll.
8. Ordinal
9. Logistic regression
10. The statistical test is appropriate for the data.

xii. The superiority of addition of ezetimibe to ongoing atorvastatin 10 mg during period I, reduced LDL-C by 22%, and adding ezetimibe to atorvastatin 20 mg during period II reduced LDL-C by 17%, and rosuvastatin reduced LDL-C by an additional 6.9% to 9.5%. Ezetimibe 10 mg plus atorvastatin 10 mg reduced LDL-C significantly more than doubling atorvastatin from 10 to 20 mg and significantly more than switching to rosuvastatin 10 mg. P <0.05; Mean (95% CI).

xiii. Overall, at least 1 AE occurred in 12.6% of patients during period I and 11.1% of patients during period II. No patient in any treatment group experienced a serious drug-related AE.

xiv. The author concluded that the treatment of hypercholesterolemia in subjects with high risk of CVD had greater reduction in percentage of LDL-C in the atorvastatin 10 mg in addition to the ezetimibe group in comparison to the rosuvastatin 10 and atorvastatin 20 mg.

xv. Power was set and met, biostatistical test was appropriate for the data type, the outcome measure is valid or accepted practice, inclusion and exclusion criteria are adequate, randomization resulted in similar groups, the treatment regimen is appropriate, blinding is sufficient to mask data, the authors conclusions are supported by the results.

xvi. Study limitations include the short duration (major limit) of the study and selection bias because the study population was mostly white.

xvii. Level l study with a major limitation (study length)

c. [brief yet logical segue to next article/presenter, if applicable]

11. RECOMMENDATION
    a. This section will evaluate the results of the articles and provide a recommendation on statin therapy in patients with dyslipidemia.
    b. SUMMARY OF EVIDENCE
        i. Article 1: Lee *et al*
            1. This study demonstrated the efficacy of combination low intensity rosuvastatin and ezetimibe compared to moderate intensity rosuvastatin.
        ii. Article 2: Catapano *et al*
            1. This study demonstrated the efficacy and safety of combination rosuvastatin/ ezetimibe compared to rosuvastatin monotherapy.
        iii. Article 3: Bays *et al*

1. The study demonstrated the efficacy and safety of the combination of ezetimibe to atorvastatin 10 & 20 mg and rosuvastatin 10mg at reducing LDL-C.

c. ANALYSIS OF EVIDENCE
   i. Article 1: Lee *et al*
      1. Randomized controlled trial– superiority study
      2. Level I study with minor limitations
   ii. Article 2: Catapano *et al*
      1. Randomized controlled trial– superiority study
      2. Level I study with minor limitations
   iii. Article 3: Bays *et al*
      1. Randomized controlled trial – superiority study
      2. Level l study with major and minor limitations

d. RECOMMENDATION
   i. Based on the literature evaluated, we recommend the combination medication rosuvastatin and ezetimibe over the use of rosuvastatin monotherapy for the treatment of dyslipidemia with the following limitations

e. APPLICATION TO PRACTICE
   i. Based on the evaluated studies, combination medication of rosuvastatin and ezetimibe is more efficacious than rosuvastatin monotherapy with p-values of <0.001.
   ii. The combination medication of rosuvastatin and ezetimibe had similar side effects to monotherapy of rosuvastatin and atorvastatin, with minimal gastrointestinal symptoms, such as dyspepsia, and no serious adverse events reported during the three studies.
   iii. The comparative cost for a combination pill of rosuvastatin and ezetimibe is around $3.00 per tablet, or $90 for a month's supply, and $1.44 per tablet of rosuvastatin monotherapy, or $43.20 for a month's supply. However, when comparing the cost of the medication and the long term benefits of using a combination therapy medication, the cost difference does not outweigh the benefits.
   iv. The use of statins has been known to be contraindicated in pregnancy, however there has been a special alert stating the use of statins in pregnancy greatly outweighs the risk in certain individuals, especially those at very high risk of cardiovascular events during pregnancy. Use in elderly should be done with caution and use in Asian populations should be with caution as there is an increased risk of rosuvastatin-associated myopathy in certain subgroups.

f. GRADING OF EVIDENCE
   i. Grade A Recommendation*ask him about this, might be Grade B due to our articles recommendation overall*

g. GUIDELINE COMPARISON
   i.
      1. [provide the AGREE II scores for the guideline as calculated in the AGREE II instructions section]
   ii. This seminar is given a Grade A recommendation.
   iii. The highest level of evidence for each article was a Level I evidence, therefore it received a Grade A recommendation.

iv. These two grades are similar because all three articles have a Level I evidence, indicating a Grade A recommendation.

12. PRESENTATION SUMMARY
    a. This is just a quick summary of the information that was just presented.
    b. SUMMARY
        i. The guideline highlights the management of dyslipidemia, utilizing various medication options and escalation of therapies.
        ii. Dyslipidemia is an imbalance of lipids in the blood and it involves a high level of low density lipoproteins and triglycerides. Dyslipidemia can lead to various complications and comorbidities, such as stroke and myocardial infarction.
        iii. The guideline-specific pharmacotherapy recommendations include statin therapy as well as escalation of therapy using an add-on therapy such as ezetimibe.
        iv. The three articles selected for this seminar aided in giving evidence that a combination medication of rosuvastatin and ezetimibe is more beneficial in lowering the LDL-C levels a greater percent than monotherapy with either rosuvastatin or atorvastatin. Additionally, the articles show that there is no drastic difference in side effects when comparing the combination medication and monotherapy.
        v. Our recommendation is to initiate patients that are resistant to monotherapy with a statin on a combination medication of rosuvastatin and ezetimibe for the management of their dyslipidemia and the prevention of progression to further complications, such as stroke or myocardial infarction with a Grade A recommendation.
    c. REFERENCES

        i. Micromedex Solutions; Hyperlipidemia; Dyslipidemia. Greenwood Village (CO): IBM Corporation; 2023 [January 18].
        ii. Raised cholesterol; World Health Organization: Global Health Observatory.
        iii. Lexi-Comp Online. Hudson, Ohio: Lexi-Comp, Inc.; Jan 29, 2012
        iv. Lee S, Kim W, Jong Hong T, *et al*. Effects of fixed-dose combination of low-intensity rosuvastatin and ezetimibe versus moderate-intensity rosuvastatin monotherapy on lipid profiles in patients with hypercholesterolemia: A randomized double-blind, multicenter phase III study.
        v. Catapano A, Vrablik M, Karpov Y, *et al*. A Phase 3 Randomized Controlled Trial to Evaluate Efficacy and Safety of New-Formulation Zenon (Rosuvastatin/Ezetimibe Fixed-Dose Combination) in Primary Hypercholesterolemia Inadequately Controlled by Statins. J Cardio Pharm Ther. 2022; 27 (1): 107-111.
        vi. Bays HE, Averna M, Majul C, et al. Efficacy and safety of ezetimibe added to atorvastatin versus atorvastatin uptitration or switching to rosuvastatin in patients with primary hypercholesterolemia. American Journal of Cardiology. 2013; 112: 1885-1895.
        vii.

13. FORUM FOR QUESTIONS
    a. That concludes our seminar regarding the management of dyslipidemia. We want to thank you for attending and listening and we would now like to open the floor for any questions.

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