METHODS OF REDUCING THE NEED FOR PERIPHERAL ARTERIAL REVASCULARIZATION IN A STATIN-TREATED SUBJECT

PRIORITY CLAIM

[0001] This application claims priority to U.S. Provisional Application No. 62/719,404 filed on August 17, 2018 the entire contents of which is incorporated herein by reference and relied upon.

BACKGROUND

[0002] Cardiovascular disease is one of the leading causes of death in the United States and most European countries. It is estimated that over 70 million people in the United States alone suffer from a cardiovascular disease or disorder including but not limited to high blood pressure, coronary heart disease, dyslipidemia, congestive heart failure and stroke.

[0003] Peripheral arterial disease is associated with cardiovascular morbidity and mortality. In Europe, more than 40 million people have peripheral arterial disease, and more than 200 million people have peripheral arterial disease worldwide. In the United States, at least 6.8 million people have peripheral arterial disease, with more than 13,000 deaths in 2015 and more than 100,000 people discharged a hospital in 2015. A better understanding of the prevalence, health burden, health care costs, and resource utilization associated with peripheral arterial disease is needed.

[0004] Lovaza®, a lipid regulating agent, is indicated as an adjunct to diet to reduce triglyceride levels in adult patients with very high triglyceride levels. Unfortunately, Lovaza® can significantly increase LDL-C and/or non-HDL-C levels in some patients. A need exists for improved treatments for cardiovascular diseases and disorders.

SUMMARY

[0004a] In one aspect, the present disclosure refers to use of a pharmaceutical composition comprising ~~about~~ 1 g to ~~about~~ 4 g of eicosapentaenoic acid ethyl ester in the manufacture of a medicament for reducing a need for peripheral arterial

revascularization in a statin-treated subject, wherein: (a) the statin-treated subject has been identified as having a fasting baseline triglyceride level of at least ~~about~~ 150 mg/dL, and (b) the composition is to be administered to the statin-treated subject per day for a period sufficient to reduce the need for peripheral arterial revascularization.

[0004b] In ~~another aspect~~one example, the present disclosure refers to a method of determining whether a subject is in need of peripheral arterial revascularization, the method comprising: (a) identifying the subject as being on a statin therapy; (b) measuring a fasting baseline triglyceride level of the subject; and (c) determining the need for peripheral arterial revascularization if the subject has a fasting baseline triglyceride level of at least about 150 mg/dL.

[0004c] In ~~yet another~~one aspect, the present disclosure refers to use of a pharmaceutical composition in the manufacture of a medicament for treating a subject at risk for peripheral arterial revascularization, wherein the pharmaceutical composition is to be administered to the subject, wherein the subject has been determined to be at risk for peripheral arterial revascularization by measuring a fasting baseline triglyceride level of the subject, and wherein the subject has a fasting baseline triglyceride level of at least about 150 mg/dL.

[0005] In some examples, the present disclosure provides methods of reducing a need for peripheral arterial revascularization in a statin-treated subject, the method comprising: (a) identifying a statin-treated subject as having a fasting baseline

CLAIMS

What is claimed is:

1. Use of a pharmaceutical composition comprising ~~about~~ 1 g to ~~about~~ 4 g of eicosapentaenoic acid ethyl ester in the manufacture of a medicament for reducing a need for peripheral arterial revascularization in a statin-treated subject, wherein:

(a) the statin-treated subject has been identified as having a fasting baseline triglyceride level of at least ~~about~~ 150 mg/dL, and

(b) the composition is to be administered to the statin-treated subject per day for a period sufficient to reduce the need for peripheral arterial revascularization.

2. The use of claim 1, wherein the composition is to be administered to the statin-treated subject in 1 to 4 dosage units per day.

3. The use of claim 1 or claim 2, wherein the eicosapentaenoic acid ethyl ester comprises at least ~~about~~ 96 wt.% of all omega-3 fatty acids in the pharmaceutical composition.

4. The use as in any one of the preceding claims, wherein the statin-treated subject has one or more of: ~~a~~ baseline non-HDL-C value of ~~about~~ 200 mg/dL to ~~about~~ 300 mg/dL; a baseline total cholesterol value of ~~about~~ 250 mg/dL to ~~about~~ 300 mg/dL; a baseline VLDL-C value of ~~about~~ 140 mg/dL to ~~about~~ 200 mg/dL; a baseline HDL-C value of ~~about~~ 10 to ~~about~~ 30 mg/dL; and/or a baseline LDL-C value of ~~about~~ 40 to ~~about~~ 100 mg/dL.

5. The use as in any one of the preceding claims, wherein the statin-treated subject is on a stable statin therapy.

6. The use of claim 5, wherein the statin therapy comprises a statin and optionally, ezetimibe, to be administered to the statin-treated subject.

7. The use as in any one of the preceding claims, further comprising identifying the statin-treated subject as having ~~LDL-control~~no clinical adverse changes in LDL levels during therapy.

8. The use as in any one of the preceding claims, wherein the statin-treated subject has a fasting baseline triglyceride level of ~~about~~ 200 mg/dL to ~~about~~ 499 mg/dL.

9. The use as in any one of claims 1 to 7, wherein the statin-treated subject has a fasting baseline triglyceride level~~s~~ of ~~about~~ 500 mg/dL to ~~about~~ 1500 mg/dL.

10. The use as in any one of claims 1 to 7, wherein the subject exhibits a reduction in a risk for cardiovascular death, coronary revascularization, unstable angina, stroke, and/or myocardial infarction.

~~11. A method of determining whether a subject is in need of peripheral arterial revascularization, the method comprising:~~

~~(a) identifying the subject as being on a statin therapy;~~

~~(b) measuring a fasting baseline triglyceride level of the subject; and~~

~~(c) determining the need for peripheral arterial revascularization if the subject has a fasting baseline triglyceride level of at least about 150 mg/dL.~~

~~12. The method of claim 11, wherein the subject has been identified at least about 5 years from receiving a least one claim for the statin therapy.~~

~~13. The method of claim 11 or claim 12, further comprising identifying the subject as having LDL-control.~~

~~14. The method as in any one of claims 11 to 13, wherein the subject has a fasting baseline triglyceride level of about 200 mg/dL to about 499 mg/dL.~~

~~15. The method as in any one of claims 11 to 13, wherein the subject has a fasting triglyceride level of about 500 mg/dL to about 1500 mg/dL.~~

~~16. The method as in any one of claims 11 to 15, wherein the subject exhibits a reduction in a risk for cardiovascular death, coronary revascularization, unstable angina, stroke, and/or myocardial infarction.~~

~~17~~11. Use of a pharmaceutical composition in the manufacture of a medicament for ~~treating~~ reducing a risk of cardiovascular events in a subject determined to be at risk for peripheral arterial revascularization~~, wherein the pharmaceutical composition is to be administered to the subject, wherein the subject has been determined to be at risk for peripheral arterial revascularization by measuring a fasting baseline triglyceride level of the subject, and wherein the subject has~~ by having a fasting baseline triglyceride level of at least ~~about~~ 150 mg/dL, wherein the pharmaceutical composition comprises 1 g to 4 g of eicosapentaenoic acid ethyl ester, and wherein the eicosapentaenoic acid ethyl ester comprises at least 96 wt.% of all omega-3 fatty acids in the medicament.

~~18~~12. The use of claim ~~17~~11, wherein the subject is on a statin therapy.

~~19. The use of claim 17 or claim 18, wherein the pharmaceutical composition comprises about 1 g to about 4 g of eicosapentaenoic acid ethyl ester.~~

~~20. The use as in any one of claims 17 to 19, wherein the eicosapentaenoic acid ethyl ester comprises at least about 96 wt.% of all omega-3 fatty acids in the pharmaceutical composition.~~

~~21~~13. The use ~~as in any one of claims 17 to 20~~of claim 11 or claim 12, wherein a peripheral arterial revascularization is to be ~~further~~ performed in addition to administration of the medicament.

~~22~~14. The use as in any one of claims ~~17~~11 to ~~21~~13, wherein the subject has a fasting baseline triglyceride level of ~~about~~ 200 mg/dL to ~~about~~ 499 mg/dL.

~~23~~15. The use as in any one of claims ~~17~~11 to ~~21~~13, wherein the subject has a fasting triglyceride level of ~~about~~ 500 mg/dL to ~~about~~ 1500 mg/dL.

~~24~~16. The use as in any one of claims ~~15~~11 to ~~23~~15, wherein the ~~subject exhibits a reduction in a risk for~~cardiovascular events include cardiovascular death, coronary revascularization, unstable angina, stroke, and/or myocardial infarction.