of various hypercholesterolemic populations including patients with type 2 diabetes mellitus and patients with muscle-related statin intolerance. The present application discloses on a method using fixed dose combination of ETC-1002 and Ezetimibe based on results from studies, disclosed herein, that compared the efficacy and safety of ETC-1002 monotherapy (120 mg or 180 mg daily) and ETC-1002 combined with Ezetimibe 10 mg (EZE) versus EZE monotherapy among hypercholesterolemic patients with or without a history of statin-related muscle symptoms.

[0006] Ezetimibe is a compound which lowers cholesterol levels in the body by decreasing cholesterol absorption in the small intestine. It can be used alone or in combination with statin therapy. Although effective for lowering the overall cholesterol count in a patient, clinical results have never shown Ezetimibe could have a statistically significant impact on major cardiovascular event outcomes, for example those associated with a heart attack or stroke. Moreover, Ezetimibe has not been shown effective for reducing atherosclerosis.

[0006a] In one aspect, provided herein is use of 180 mg ETC-1002 and 10 mg Ezetimibe in the manufacture of a medicament for preventing or reducing the risk of myocardial infarction in a subject with cardiovascular disease or at risk of developing cardiovascular disease.

[0007] The inventors have found that both Ezetimibe and ETC-1002 directly affect a lower LDL-C level (within 2 weeks) in patients which are statin-tolerant and in patients which are statin-intolerant. Additionally, the inventors find that combining these two therapies leads to cooperative activity, even lower LDL-C levels, and a favorable clinical treatment. Accordingly, the present disclosure is directed toward cholesterol-lowering compositions comprising Ezetimibe and ETC-1002. These compositions lead to further reductions in total cholesterol, and specifically LDL-C, in patients.

[0008] The present application also discloses a method of lowering cholesterol using fixed dose combination of ETC-1002 and Ezetimibe. Based on observations in on-going studies, combination therapy with ETC-1002 and a fixed dosage of Ezetimibe has comparable efficacy and safety to that of ETC-1002 alone, or combined with a fixed, low to medium dosage of one or more statins. Of course, combination therapy with a fixed dosage ETC-1002 and Ezetimibe is also significantly greater versus statin or ETC-1002 monotherapy (120 mg or 180 mg daily) in patients with or without a history of statin-related muscle symptoms. The combination therapy shows a significantly greater efficacy and safety profile even in acute hypercholesterolemic patients.

[0009] In one example, methods and compositions of present disclosure even lower cholesterol (LDL-C, and other markers for example: triglycerides, ApoB, hsCRP, non-HDL-C, HDL-C, LDL particle number, ApoA1, and lower the risk of cardiovascular disease and

CLAIMS

What is claimed:

1. Use of 180 mg ETC-1002 and 10 mg Ezetimibe in the manufacture of a medicament for preventing or reducing the risk of myocardial infarction in a subject with cardiovascular disease or at risk of developing cardiovascular disease.

2. The use of claim 1, wherein the subject has cardiovascular disease.

3. The use of claim 1, wherein the subject does not have cardiovascular disease.

4. The use of claim 1, wherein the medicament is a fixed-dose combination.

5. The use of claim 1, wherein the subject is human.