committee -- illustrated a significant reduction of events compared to placebo and SGLT2 inhibitors [HR = 0.40 (95% CI, 0.16 – 1.00; p=0.05)].

Brief Description of the Disclosure

[0009] The present disclosure provides methods of treating and/or preventing Major adverse cardiovascular events (MACE) (including non-fatal myocardial infarction, cardiovascular death, stroke, and hospitalization for CVD events) by administering to a subject in need thereof, a sodium-glucose transport protein 2 (SGLT2) inhibitor and a compound of Formula I or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof.

[0009a] In an aspect, there is provided the use of a sodium-glucose transport protein 2 (SGLT2) inhibitor and 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof,

in the manufacture of a medicament for treating and/or preventing major adverse cardiovascular events (MACE) in a subject in need thereof, wherein the subject is on statin therapy.

[0009b] In another aspect, there is provided the use of a sodium-glucose transport protein 2 (SGLT2) inhibitor and 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof,

in the manufacture of a medicament for treating and/or preventing any individual component of major adverse cardiovascular events (MACE) in a subject in need thereof, wherein the subject is on statin therapy.

[0009c] In another aspect, there is provided a medicament comprising sodium-glucose transport protein 2 (SGLT2) inhibitor and 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-

dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof for use in therapy in a subject in need thereof, wherein the subject is on statin therapy.

[0010] In some examples, the disclosure provides methods of preventing cardiovascular death by administering to a subject in need thereof, a sodium-glucose transport protein 2 (SGLT2) inhibitor and a compound of Formula I or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof.

[0011] In some examples, the disclosure provides methods of treating and/or preventing hospitalization for CVD events by administering to a subject in need thereof, a sodium-glucose transport protein 2 (SGLT2) inhibitor and a compound of Formula I or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof.

[0012] In some examples, the disclosure provides methods of treating and/or preventing a non-fatal myocardial infarction by administering to a subject in need thereof, a sodium-glucose transport protein 2 (SGLT2) inhibitor and a compound of Formula I or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof.

[0013] In some examples, the compound of Formula I is administered simultaneously with a SGLT2 inhibitor. In some examples, the Compound of Formula I is administered sequentially with the SGLT2 inhibitor. In some examples, the Compound of Formula I is administered in a single pharmaceutical composition with the SGLT2 inhibitor. In some examples, the Compound of Formula I and the SGLT2 inhibitor are administered as separate compositions.

[0014] In some examples, the compound of Formula Ia is selected from

Claims

1. Use of a sodium-glucose transport protein 2 (SGLT2) inhibitor and 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof, in the manufacture of a medicament for treating and/or preventing major adverse cardiovascular events (MACE) in a subject in need thereof, wherein the subject is on statin therapy.
2. Use of a sodium-glucose transport protein 2 (SGLT2) inhibitor and 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof, in the manufacture of a medicament for treating and/or preventing any individual component of major adverse cardiovascular events (MACE) in a subject in need thereof, wherein the subject is on statin therapy.
3. A medicament comprising sodium-glucose transport protein 2 (SGLT2) inhibitor and 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof for use in therapy in a subject in need thereof, wherein the subject is on statin therapy.
4. The use according to claim 1 or 2, or medicament according to claim 3, wherein the medicament comprises 200 mg of 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one or an equivalent amount of a pharmaceutically acceptable salt thereof.
5. The use according to claim 1 or 2 or medicament according to claim 3, wherein the medicament comprises 100 mg of 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one or an equivalent amount of a pharmaceutically acceptable salt thereof.
6. The use according to any one claim of claims 1, 2, 4, and 5, or the medicament according to claim 3, wherein the SGLT2 inhibitor is selected from empagliflozin, canagliflozin, remogliflozin, ipragliflozin, HM41322, and dapagliflozin.

7. The use according to any one claim of claims 1, 2, 4, and 5, or the medicament according to claim 3, wherein the SGLT2 inhibitor is selected from bexagliflozin, ertugliflozin, sotagliflozin, luseogliflozin, and tofogliflozin.
8. The use according to any one claim of claims 1, 2, and 4-7, wherein the subject is a human.
9. The use according to any one claim of claims 1, 2, and 4-8, wherein the subject is a human with type 2 diabetes and low HDL cholesterol (below 40mg/dL for males and below 45 mg/dL for females) and a recent acute coronary syndrome (ACS) (preceding 7-90 days).
10. The use according to any one claim of claims 1, 2 and 4-9, wherein the MACE is selected from non-fatal myocardial infarction, cardiovascular death, stroke, and hospitalization for cardiovascular disease events.
11. The use according to claim 10, wherein the hospitalization for cardiovascular disease events is hospitalization for congestive heart failure.
12. The use according to any one claim of claims 1, 2 and 4-9, wherein the MACE is selected from non-fatal myocardial infarction, cardiovascular death, and stroke.
13. The use according to any one claim of claims 1, 2, and 4-12, wherein 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof is administered before the SGLT2 inhibitor.
14. The use according to any one claim of claims 1, 2, and 4-12, wherein 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof is administered simultaneously with the SGLT2 inhibitor.
15. The use according to any one claim of claims 1, 2, and 4-12, wherein 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof is administered after the SGLT2 inhibitor.
16. The use according to any one claim of claims 1, 2, 4-12, and 14, wherein 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or

RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof is administered in a single pharmaceutical composition with the SGLT2 inhibitor.

17. The use according to any one claim of claims 1, 2, and 4-15, wherein 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof and the SGLT2 inhibitor are administered in separate pharmaceutical compositions.