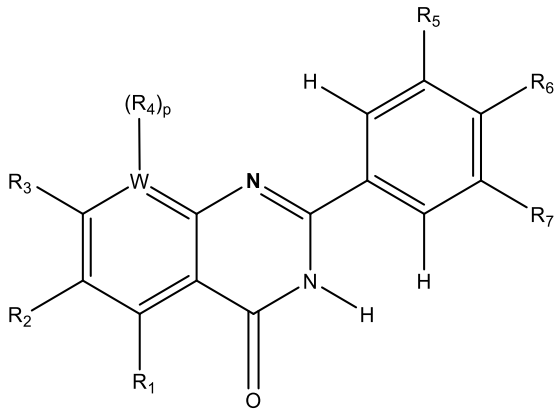
Claims

1. Use of ~~A method for treating and/or preventing major adverse cardiovascular events (MACE) comprising 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, wherein:



Formula I

R_1 and R_3 are each independently selected from alkoxy, alkyl, amino, halogen, and hydrogen;

R_2 is selected from alkoxy, alkyl, alkenyl, alkynyl, amide, amino, halogen, and hydrogen;

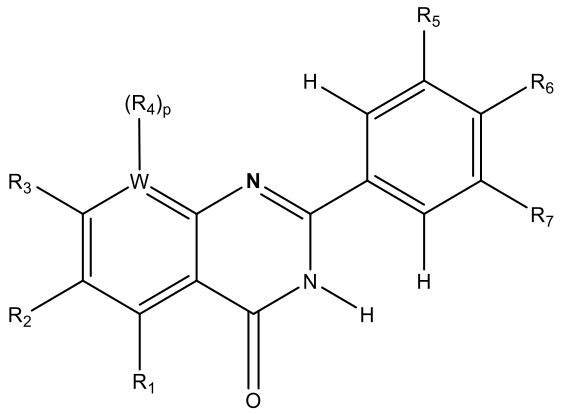
R_5 and R_7 are each independently selected from alkyl, alkoxy, amino, halogen, and hydrogen;

R_6 is selected from amino, amide, alkyl, hydrogen, hydroxyl, piperazinyl, and alkoxy;

W is selected from C and N, wherein if W is N, then p is 0 or 1, and if W is C, then p is 1; and for W-$(R_4)_p$, W is C, p is 1 and R_4 is H, or W is N and p is 0,

in the manufacture of a medicament for treating and/or preventing major adverse cardiovascular events (MACE) in a subject in need thereof.

2. ~~A method for treating and/or preventing any individual component of MACE comprising administrating to a subject in need thereof,~~Use of a sodium-glucose transport protein 2 (SGLT2) inhibitor and a compound of Formula I or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof, wherein:



Formula I

R_1 and R_3 are each independently selected from alkoxy, alkyl, amino, halogen, and hydrogen;

R_2 is selected from alkoxy, alkyl, alkenyl, alkynyl, amide, amino, halogen, and hydrogen;

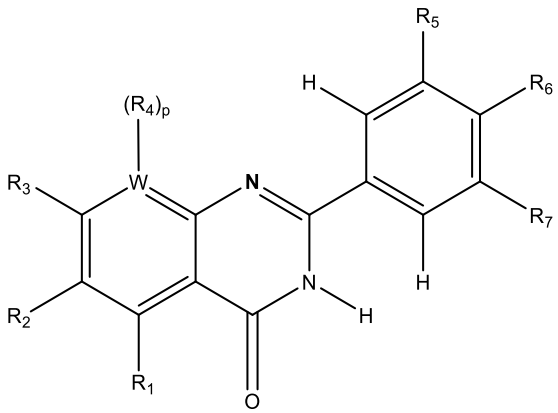
R_5 and R_7 are each independently selected from alkyl, alkoxy, amino, halogen, and hydrogen;

R_6 is selected from amino, amide, alkyl, hydrogen, hydroxyl, piperazinyl, and alkoxy;

W is selected from C and N, wherein if W is N, then p is 0 or 1, and if W is C, then p is 1; and for W-$(R_4)_p$, W is C, p is 1 and R_4 is H, or W is N and p is 0,

in the manufacture of a medicament for treating and/or preventing any individual component of MACE in a subject in need thereof.

3. The ~~method~~ use of claim 1 or claim 2, wherein the compound of Formula I is selected from compounds of Formula 1a:



Formula Ia

or a stereoisomer, tautomer, pharmaceutically acceptable salt, or hydrate thereof,

wherein:

R_1 and R_3 are each independently selected from alkoxy, alkyl, and hydrogen;

R_2 is selected from alkoxy, alkyl, and hydrogen;

R_5 and R_7 are each independently selected from alkyl, alkoxy, and hydrogen;

R_6 is selected from alkyl, hydroxyl, and alkoxy;

W is selected from C and N, wherein if W is N, then p is 0 or 1, and if W is C, then p is 1; and

for W-$(R_4)_p$, W is C, p is 1 and R_4 is H, or W is N and p is 0.

4. The ~~method~~ use of any one of claims 1 to 3, wherein the compound of Formula I or Ia is 2-(4-(2-hydroxyethoxy)-3,5-dimethylphenyl)-5,7-dimethoxyquinazolin-4(3H)-one (RVX-208 or RVX000222) or a pharmaceutically acceptable salt thereof.
5. The ~~method~~ use according to any one claim of claims 1 to 4, comprising ~~administering~~ a daily dose of 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 to be administered to a subject in need thereof.
6. The ~~method~~use of claim 5, wherein a subject in need thereof is to be administered 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 twice daily.
7. The ~~method~~ use according to any one claim of claims 1 to 6, wherein the SGLT2 inhibitor is selected from empagliflozin, canagliflozin, remogliflozin, ipragliflozin, HM41322, and dapagliflozin.
8. The ~~method~~ use according to any one claim of claims 1 to 6, wherein the SGLT2 inhibitor is selected from bexagliflozin, ertugliflozin, sotagliflozin, luseogliflozin, and tofogliflozin.
9. The ~~method~~ use according to any one claim of claims 1 to 8, wherein the subject is a human.
10. The ~~method~~ use according to any one claim of claims 1 to 9, 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).

11. The ~~method~~use according to any one claim of claims 1-10, wherein the subject is on statin therapy.
12. The ~~method~~ use according to any one of claims 1-11, wherein the MACE is selected from non-fatal myocardial infarction, cardiovascular death, stroke, and hospitalization for cardiovascular disease events.
13. The ~~method~~ use according to claim 12, wherein the cardiovascular disease event is congestive heart failure.
14. The ~~method~~ use according to claim 12, wherein the hospitalization for cardiovascular disease events is hospitalization for congestive heart failure.
15. The ~~method~~ use according to any one of claims 1-11, wherein the MACE is selected from non-fatal myocardial infarction, cardiovascular death, and stroke.