cardiovascular risk increase of 11-16%, a [total cholesterol]/[HDL] ratio of 4.22-5.53 resulted in a cardiovascular risk increase of 19-29%, and a [total cholesterol]/[HDL] ratio of 5.54-18.1 resulted in a cardiovascular risk increase of 26-33% (Nam et al., 2006).

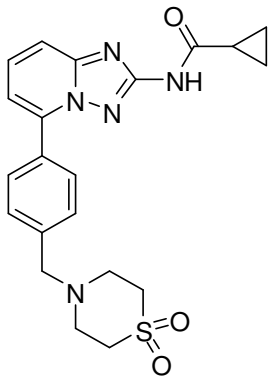
[0031] Typically, in a recent treatment study with Tofacitinib, a JAK inhibitor for 6 weeks at a dose of 10 mg bid in RA patient, the atherogenic index was unchanged before and after treatment at about 3.5 (Charles-Schoeman et al., 2015) thus leaving the patient at an increased cardiovascular risk before and after treatment. In contrast, upon administration of Compound 1 at doses ranging from 50 mg to 200 mg (once or twice daily) for a period of at least 4 weeks resulted in a drop of the atherogenic index, thereby reducing the initial cardiovascular risk.

[0032] Furthermore, this effect was sustained over at least 12 weeks, and at least 24 weeks and were observed over a dose range of 50-200 mg administered either twice daily (b.i.d) or once a day (q.d.).

[0033] Additionally, this effect was seen both in healthy volunteers, and patients suffering from inflammatory diseases (for example RA and Crohn's disease).

[0034] Therefore Compound 1 would be particularly advantageous in preventing and/or treating cardiovascular disorder, and the object of the present disclosure is Compound 1 for use in the prophylaxis and/or treatment of cardiovascular disorder and/or dyslipidemia.

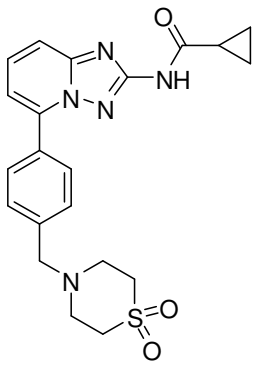
[0035] Accordingly, disclosed is the compound of the disclosure having a Formula (I):



I

is provided for use is the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia.

[0035a] In one aspect, the present invention provides a use of a compound according to Formula I:



I

or a pharmaceutically acceptable salt thereof, or a solvate or the salt of a solvate thereof, or an active metabolite thereof in the manufacture of a medicament for the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia.

[0036] Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of chronic cardiovascular disorders. In a more particular example, the cardiovascular disorder is atherosclerosis.

[0037] Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of chronic dyslipidemia. In a more particular example, the cardiovascular disorder is hypolipidemia.

[0038] Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of cardiovascular disorders in patients not suffering from RA as measured by the DAS28(CRP) score method (Wells et al., 2008), wherein the DAS28(CRP) value is less than 2.6.

[0039] Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of cardiovascular disorders in RA patients, wherein the treatment extends for longer than 4 weeks.

[0040] Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of cardiovascular disorders in IBD patients. Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of cardiovascular disorders in ulcerative colitis and/or Crohn's disease patients. Also disclosed is the compound of the disclosure for use in the prophylaxis and/or treatment of cardiovascular disease in Crohn's disease patients.

[0041] Also disclosed are pharmaceutical compositions comprising a compound of the disclosure, and a suitable pharmaceutical carrier, excipient or diluent for use in the prophylaxis and/or treatment of cardiovascular disorders. In a more particular example, the cardiovascular disorder is atherosclerosis.

[0041a] In another aspect, the present invention provides a use of a pharmaceutical composition comprising the compound according to Formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, excipient, or diluent in the manufacture of a medicament for the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia.

[0042] The present disclosure also provides pharmaceutical compositions comprising a compound of the disclosure, and a suitable pharmaceutical carrier, excipient or diluent for use in the prophylaxis and/or treatment of dyslipidemia. In a more particular example, the cardiovascular disorder is hypolipidemia.

[0043] . In a further particular example, the pharmaceutical composition may additionally comprise further therapeutically active ingredients suitable for use in combination with the compounds of the disclosure. In a more particular example, the further therapeutically active ingredient is an agent for the treatment of cardiovascular disorders.

[0044] In a further particular example, the pharmaceutical composition may additionally comprise further therapeutically active ingredients suitable for use in combination with the compounds of the disclosure. In a more particular example, the further therapeutically active ingredient is an agent for the treatment of dyslipidemia.

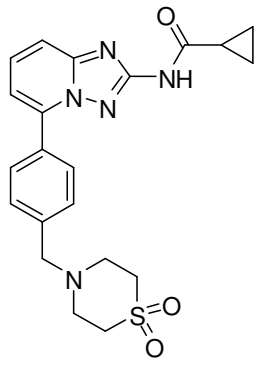
[0045] Moreover, the compounds of the disclosure, useful in the pharmaceutical compositions and treatment methods disclosed herein, are pharmaceutically acceptable as prepared and used.

[0046] Also disclosed is a method for the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia in a mammal in need thereof, in particular humans, which method comprises administering an effective amount of the pharmaceutical composition or compounds of the disclosure as described herein.

[0047] Also disclosed is a method of decreasing the risk of cardiovascular risk in a mammal, in particular humans, which method comprises

CLAIMS

1) Use of a compound according to Formula I:



I

or a pharmaceutically acceptable salt thereof, or a solvate or the salt of a solvate thereof, or an active metabolite thereof in the manufacture of a medicament for the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia.

2) The use according to claim 1, wherein said salt of a solvate is a [Compound according to Formula I:HCl:3H_2O] adduct.

3) The use according to claim 1 or 2, wherein the cardiovascular disorder is atherosclerosis.

4) The use according to claim 1, 2 or 3, for use in combination with a further therapeutic agent.

5) Use of a pharmaceutical composition comprising the compound according to Formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, excipient, or diluent in the manufacture of a medicament for the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia.

6) The use according to claim 5, wherein the composition comprises a further therapeutic agent.

7) The use according to any one of claims 1 to 6, wherein the medicament is to be used in an individual presenting an abnormal lipid profile.

8) The use according to claim 7, wherein the abnormal lipid level is characterized by [LDL] below 50 mg/dL (or below 1.3 mmol/L) and [HDL] below 40 mg/dL (or below 1.04 mmol/L).

9) The use according to any one of claims 1 to 4 and 6 to 7, wherein the medicament is to be used in a clinical non RA-afflicted patient.

10) The use according to any one of claims 1 to 4 and 6 to 7, wherein the medicament is to be used in a clinical non RA-afflicted patient, wherein the non RA-afflicted condition is measured by the DAS28(CRP) score.

11) The use according to any one of claims 1 to 4 and 6 to 7, wherein the medicament is to be used in a clinical non RA-afflicted patient, wherein the non RA-afflicted condition is measured by the DAS28(CRP) score, wherein the DAS28(CRP) score is less than 2.6.

12) The use according to any one of claims 1 to 4 and 6 to 7, wherein the medicament is to be used in a clinical non RA-afflicted patient, wherein the non RA-afflicted condition is measured by the DAS28(CRP) score, and having a CRP level greater than 3 mg/L.

13) The use according to any one of claims 1 to 4 and 6 to 7, wherein the medicament is to be used in a clinical RA-afflicted patient, wherein the compound or pharmaceutical composition is to be administered at least once a week over a period of greater than 4 weeks.

14) The use according any one of claims 1 to 4 and 6 to 7, wherein the medicament is to be used in a clinical RA-afflicted patient, wherein the clinical RA-afflicted patient condition is measured by the DAS28(CRP) score.

15) The use according to claim 14, wherein the DAS28(CRP) score is greater than 3.2.

16) The use according to any one of claims 1-15, wherein said compound, or pharmaceutically acceptable salt thereof is to be administered at a dose of 100 mg twice a day.

17) The use according to any one of claims 1-15, wherein said compound, or pharmaceutically acceptable salt thereof is to be administered at a dose of 200 mg once a day.

18) Use of a dose of the compound according to Formula I, or a pharmaceutically acceptable salt thereof comprised between 25 mg and 400 mg in the manufacture of a medicament for the prophylaxis and/or treatment of cardiovascular disorders and/or dyslipidemia, wherein the compound is to be administered to an individual, wherein the determination of the dose comprising the steps of:

- measuring the DAS28(CRP) levels of an individual by performing a 28 tender and swollen joint count, CRP measurement from blood analysis, and a general health assessment on a visual analog scale,

- comparing said DAS28(CRP) level to the disease scoring index wherein a score below 2.6 is indicative of remission , a score between 2.6 and 3.2 is indicative of low disease activity, a score between 3.2 and 5.1 is indicative of moderate disease activity, and a score above 5.1 is linked to high disease activity.

19) The use according to claim 4 or according to claim 6, wherein the further therapeutic agent is an agent for the prophylaxis and/or treatment of cardiovascular disease.

20) The use according to claim 4 or according to claim 6, wherein the further therapeutic agent is an agent for the prophylaxis and/or treatment of atherosclerosis.