SUMMARY

[0005a] In one aspect of the present disclosure, there is provided a use of relacorilant in the manufacture of a medicament for treating a disorder in a patient, wherein said patient is to be administered:

a) an effective dose of relacorilant; and

b) an effective dose of a therapeutic agent, wherein said therapeutic agent is a substrate for CYP2C8 enzyme metabolism, said therapeutic agent having a single agent dose when administered without other pharmaceutical agents, wherein said therapeutic agent effective dose is substantially the same as said single agent dose;

wherein a) and b) are performed at times effective to provide the patient with an effective level of relacorilant and an effective level of the therapeutic agent at the same time,

whereby the disorder is treated.

[0005b] In another aspect of the present disclosure, there is provided a use of relacorilant in the manufacture of a medicament for treating cancer in a patient, wherein said patient is to be administered:

a) relacorilant, and

b) an anticancer agent, wherein said anticancer agent is a substrate for CYP2C8 enzymes, the anticancer agent having a therapeutic dose when it is to be administered to a subject in the absence of other pharmaceutical agents, and wherein said anticancer agent is to be administered to the patient at a dose that is substantially the same as said therapeutic dose.

[0005c] In a further aspect of the present disclosure, there is provided a use of relacorilant and a CYP2C8 substrate in the manufacture of a medicament for the treatment of a disorder, wherein relacorilant and a CYP2C8 substrate are used concomitantly, wherein CYP2C8 substrate alone has been used in treating said disorder, and wherein the amount of said CYP2C8 substrate used in said concomitant treatment with relacorilant is the same amount of CYP2C8 substrate as used alone in treating said disorder.

[0006] Many therapeutic drugs are substrates of CYP2C8 enzymes; an otherwise safe dose of a first drug metabolized by CYP2C8 may be a toxic dose when concomitantly administered with a second drug that is a CYP2C8 inhibitor. *In vitro* studies are used to indicate drug combinations expected to suffer from such negative drug-drug interactions (DDIs).

[0007] Relacorilant is believed to be useful in treating many disorders, including cancer and hypercortisolism. Relacorilant is further believed to be useful in combination treatments for cancer and in treating hypercortisolism. *In vitro* tests demonstrated that relacorilant is a potent inhibitor of CYP2C8 (IC_{50} of 0.21 μM). Such potent inhibition of CYP2C8 would be expected to increase plasma exposure of CYP2C8 substrates by more than five-fold when co-administered with relacorilant. Thus, it was expected that significant reductions in doses of CYP2C8 substrates (e.g., pioglitazone, rosiglitazone, enzalutamide, and others) would be required when administered in combination with relacorilant.

[0008] Surprisingly, Applicant determined that it was safe to co-administer relacorilant and a CYP2C8 substrate to human subjects without modifying the dose of the CYP2C8 substrate. Applicant discloses herein that relacorilant may be safely administered along with unmodified doses of pioglitazone, and other CYP2C8 substrates, such as, e.g., rosiglitazone, and enzalutamide. Relacorilant and unmodified doses of enzalutamide may be administered for the treatment of cancer, e.g., prostate cancer. Relacorilant and unmodified doses of pioglitazone or rosiglitazone may be administered for the treatment of cancer, or hypercortisolism.

[0009] Accordingly, Applicant discloses herein that a CYP2C8 substrate may be concomitantly administered with the selective glucocorticoid receptor modulator relacorilant without reduction in the dose of the CYP2C8 substrate. Such concomitant administration of a CYP2C8 substrate and relacorilant is believed to be safe for the subject and to provide the therapeutic benefits of both drugs to the subject. In examples, the CYP2C8 substrate is pioglitazone, rosiglitazone or enzalutamide.

[0010] The methods disclosed herein surprisingly provide safe methods for administering drug combinations that were previously expected to be unsafe, allowing concomitant administration of drug combinations with relacorilant. Such drug combinations are believed to provide more effective treatments than treatment with only one of the drugs in the absence of the other. The surprising ability to safely administer these drug combinations provide

CLAIMS

1. Use~~A method~~ of relacorilant in the manufacture of a medicament for treating a disorder in a patient, wherein said patient is to be administered~~the method comprising administering to a patient in need of treatment for said disorder~~:

a) an effective dose of relacorilant; and

b) an effective dose of a therapeutic agent, wherein said therapeutic agent is a substrate for CYP2C8 enzyme metabolism, said therapeutic agent having a single agent dose when administered without other pharmaceutical agents, wherein said therapeutic agent effective dose is substantially the same as said single agent dose;

wherein~~Wherein~~ a) and b) are performed at times effective to provide the patient with an effective level of relacorilant and an effective level of the therapeutic agent at the same time,

whereby~~Whereby~~ the disorder is treated.

2. The use~~method~~ of claim 1, wherein the relacorilant dose is between about 1 milligram per kilogram (mg/kg) and about 20 mg/kg.

3. The use~~method~~ of claim 1, wherein the relacorilant dose is between about 50 mg and about 500 mg.

4. The use~~method~~ of claim 4, wherein the relacorilant dose is to be administered at a time within about 15 minutes of the time of administration of the therapeutic agent dose.

5. The use~~method~~ of claim 1, wherein the relacorilant dose and therapeutic agent dose are to be administered sequentially.

6. The use~~method~~ of claim 5, wherein the relacorilant dose is to be administered to the patient, and then, after a time interval, the therapeutic agent dose is to be administered to the patient.

7. The use~~method~~ of claim 5, wherein the therapeutic agent dose is to be administered to the patient, and then, after a time interval, the relacorilant dose is to be administered to the patient.

8. The use~~method~~ of claim 6, wherein said time interval is selected from about one hour and about one day.

9. The use~~method~~ of claim 7, wherein said time interval is selected from about one hour and about one day.

10. The use~~method~~ of claim 1, wherein the therapeutic agent is selected from rosiglitazone, pioglitazone, and enzalutamide.

11. The use~~method~~ of claim 1, wherein said disorder is cancer.

12. The use~~method~~ of claim 11, wherein said disorder is prostate cancer.

13. The use~~method~~ of claim 12, wherein the therapeutic agent is enzalutamide.

14. The use~~method~~ of claim 1, wherein said disorder is hypercortisolism.

15. The use~~method~~ of claim 14, wherein the therapeutic agent is selected from rosiglitazone and pioglitazone.

16. Use~~A method~~ of relacorilant in the manufacture of a medicament for treating cancer in a patient~~, the method comprising administering to a patient~~ wherein said patient is to be administered ~~in need of cancer treatment~~:

a) relacorilant, and

b) an anticancer agent, wherein said anticancer agent is a substrate for CYP2C8 enzymes, the anticancer agent having a therapeutic dose when it is to be administered to a subject in the absence of other pharmaceutical agents, and wherein said anticancer agent is to be administered to the patient at a dose that is substantially the same as said therapeutic dose.

17. The use~~method~~ of claim 16, wherein said relacorilant is to be administered to said patient at a dosage of between about 1 milligram per kilogram (mg/kg) and about 20 mg/kg.

18. The use~~method~~ of claim 16, wherein said relacorilant is to be administered to said patient at a dose of between about 75 mg and about 200 mg per day.

19. The use~~method~~ of claim 16, wherein said relacorilant and said anticancer agent are to be administered to the patient at substantially the same time.

20. The use~~method~~ of claim 16, wherein said relacorilant and said anticancer agent are to be administered sequentially to the patient.

21. The usemethod of claim 20, wherein said anticancer agent is to be administered to the patient, and then, after a time interval, said relacorilant is to be administered to the patient.

22. The usemethod of claim 20, wherein said relacorilant is to be administered to the patient, and then, after a time interval, said anticancer agent is to be administered to the patient.

23. The usemethod of claim 21, wherein said time interval is selected from about one hour and about one day.

24. The usemethod of claim 22, wherein said time interval is selected from about one hour and about one day.

25. UseThe concomitant use of relacorilant and a CYP2C8 substrate in the manufacture of a medicament for the treatment of a disorder, wherein relacorilant and a CYP2C8 substrate are used concomitantly, wherein CYP2C8 substrate alone has been used in treating said disorder, and wherein the amount of said CYP2C8 substrate used in said concomitant treatment with relacorilant is the same amount of CYP2C8 substrate as used alone in treating said disorder.

26. The use of claim 25, wherein the amount of relacorilant is between about 50 mg and about 1500 mg.

27. The use of claim 25, wherein the CYP2C8 substrate is selected from rosiglitazone, pioglitazone, and enzalutamide.

28. The use of claim 25, wherein said disorder is cancer.

29. The use of claim 28, wherein said disorder is prostate cancer, and wherein the CYP2C8 substrate is enzalutamide.

30. The use of claim 27, wherein said disorder is hypercortisolism, and wherein the CYP2C8 substrate is selected from rosiglitazone and pioglitazone.