clinical trials in patients with Cushing's syndrome and in patients with various types of cancer including ovarian cancer and pancreatic cancer.

SUMMARY

[0005a] In one 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 the patient is to be administered paclitaxel and relacorilant according to a 28-day schedule:

a) an effective dose of relacorilant that is to be administered the day before, the day of and the day after the paclitaxel administration; and

b) an effective dose of paclitaxel to be administered on days 1, 8, and 15 of said 28-day schedule, wherein said paclitaxel has a single agent dose of 100 mg/m^2 to 125 mg/m^2 when administered without other pharmaceutical agents, wherein said effective dose of paclitaxel is reduced by 20% to 35% from said single agent dose of paclitaxel when co-administered with relacorilant;

wherein a) and b) are to be administered at times effective to provide the patient with an effective level of relacorilant and an effective level of paclitaxel at the same time,

whereby the cancer 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 the patient is to be administered paclitaxel and relacorilant according to a 28-day schedule:

a) an effective dose of relacorilant that is to be administered the day before, the day of and the day after the paclitaxel administration; and

b) an effective dose of paclitaxel, wherein said paclitaxel has a single agent dose of 100 mg/m^2 to 125 mg/m^2 when administered without other pharmaceutical agents, wherein said effective dose of paclitaxel is between 60 mg/m^2 to 95 mg/m^2 when co-administered with relacorilant;

wherein a) and b) are to be administered at times effective to provide the patient with an effective level of relacorilant and an effective level of paclitaxel at the same time,

whereby the cancer is treated.

[0006] Many therapeutic drugs are substrates of CYP2C8 enzymes, CYP3A4 enzymes, or both; an otherwise safe dose of a first drug metabolized by these CYP enzymes may be a

toxic dose when concomitantly administered with a second drug that is an inhibitor of the CYP enzyme. Where a therapeutic drug's primary route of elimination is through metabolism by both CYP2C8 and CYP3A4 enzymes, administration of a concomitant drug that inhibits of both CYP2C8 and CYP3A4 would be expected to cause a substantial increase in the plasma levels of the therapeutic drug by blocking its only elimination pathways. Co-administration with a dual inhibitor of CYP2C8 and CYP3A4 would lead to a greater magnitude of drug-drug interactions (DDIs) versus co-administration with an inhibitor of only one of the enzymes. *In vitro* studies are used to indicate drug combinations expected to suffer from such negative 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) and a potent inhibitor of CYP3A4 (IC_{50} of 1.32 μM). Such potent dual inhibition of both CYP2C8 and CYP3A4 would be expected to increase plasma exposure of dual CYP2C8 and CYP3A4 substrates by more than five-fold when co-administered with relacorilant. Thus, it was expected that significant reductions in doses of dual CYP2C8 and CYP3A4 substrates (e.g., paclitaxel) would be required when administered in combination with relacorilant.

[0008] Upon co-administration with relacorilant such potent inhibition of both CYP2C8 and CYP3A4 by relacorilant would be expected to increase plasma exposure of paclitaxel by blocking its primary pathway of elimination through CYP2C8- and CYP3A4-mediated metabolism. Thus, it was expected that significant reductions in paclitaxel dose would be required when administered in combination with relacorilant. On the basis of relacorilant's expected effect on paclitaxel metabolism, co-administration of paclitaxel and relacorilant would have been expected to require potential reductions in paclitaxel dose by 5-fold or more when paclitaxel is administered with relacorilant.

CLAIMS

1. Use of relacorilant in the manufacture of a medicament for treating cancer in a patient, wherein the patient is to be administered paclitaxel and relacorilant according to a 28-day schedule:

a) an effective dose of relacorilant that is to be administered the day before, the day of and the day after the paclitaxel administration; and

b) an effective dose of paclitaxel to be administered on days 1, 8, and 15 of said 28-day schedule, wherein said paclitaxel has a single agent dose of 100 mg/m^2 to 125 mg/m^2 when administered without other pharmaceutical agents, wherein said effective dose of paclitaxel is reduced by 20% to 35% from said single agent dose of paclitaxel when co-administered with relacorilant;

wherein a) and b) are to be administered at times effective to provide the patient with an effective level of relacorilant and an effective level of paclitaxel at the same time,

whereby the cancer is treated.

2. The use of claim 1, wherein said effective dose of paclitaxel is reduced from said single agent dose of paclitaxel by an amount selected from 20%, 25%, 30%, and 35%, when co-administered with relacorilant.

3. The use of claim 1, wherein said effective dose of paclitaxel is reduced from said single agent dose of paclitaxel to an effective dose of paclitaxel selected from 72 mg/m^2, 75 mg/m^2, 80 mg/m^2, 83 mg/m^2, 88 mg/m^2, 94 mg/m^2, and 96 mg/m^2 of paclitaxel.

4. The use of claim 1, wherein paclitaxel is in the form of nab-paclitaxel.

5. The use of claim 1, wherein said effective dose of relacorilant is between 75 milligrams per day (mg/day) and 200 mg/day of relacorilant.

6. The use of claim 5, wherein said effective dose of relacorilant is selected from 75 mg/day, 100 mg/day, 125 mg/day, 150 mg/day, 175 mg/day, and 200 mg/day of relacorilant.

7. The use of claim 1, wherein said cancer comprises a solid tumor.

8. The use of claim 1, wherein said cancer is selected from ovarian cancer, pancreatic cancer, prostate cancer, esophageal cancer, and melanoma.

9. The use of claim 1, wherein said cancer is ovarian cancer or pancreatic cancer.

10. The use of claim 1, wherein said relacorilant is to be administered orally.

11. The use of claim 1, wherein the doses of relacorilant and of paclitaxel are to be administered according to a 28-day schedule, wherein paclitaxel is in the form of nab-paclitaxel, and wherein the dose of nab-paclitaxel is selected from 60 mg/m^2, 72 mg/m^2, 75 mg/m^2, 80 mg/m^2, and 83 mg/m^2 of nab-paclitaxel to be administered by intravenous infusion on days 1, 8 and 15 of each 28-day cycle.

12. The use of claim 11, wherein relacorilant is to be administered the day before, the day of and the day after nab-paclitaxel administration.

13. The use of claim 12, wherein relacorilant is to be administered the day before, the day of and the day after nab-paclitaxel administration at a dose selected from 75, mg, 100 mg, 150 mg, 175 mg, 200 mg, and 200 mg of relacorilant.

14. Use of relacorilant in the manufacture of a medicament for treating cancer in a patient, wherein the patient is to be administered paclitaxel and relacorilant according to a 28-day schedule:

a) an effective dose of relacorilant that is to be administered the day before, the day of and the day after the paclitaxel administration; and

b) an effective dose of paclitaxel, wherein said paclitaxel has a single agent dose of 100 mg/m^2 to 125 mg/m^2 when administered without other pharmaceutical agents, wherein said effective dose of paclitaxel is between 60 mg/m^2 to 95 mg/m^2 when co-administered with relacorilant;

wherein a) and b) are to be administered at times effective to provide the patient with an effective level of relacorilant and an effective level of paclitaxel at the same time,

whereby the cancer is treated.

15. The use of claim 14, wherein said paclitaxel is in the form of nab-paclitaxel.

16. The use of claim 14, wherein said effective dose of paclitaxel is selected from 60 mg/m^2, 65 mg/m^2, 70 mg/m^2, 75 mg/m^2, 80 mg/m^2, 85 mg/m^2, 90 mg/m^2, and 95 mg/m^2 of paclitaxel.

17. The use of claim 14, wherein said effective dose of relacorilant is between 75 milligrams per day (mg/day) and 200 mg/day of relacorilant.

18. The use of claim 14, wherein said effective dose of relacorilant is selected from 75 mg/day, 100 mg/day, 125 mg/day, 150 mg/day, 175 mg/day, and 200 mg/day of relacorilant.

19. The use of claim 14, wherein said cancer comprises a solid tumor.

20. The use of claim 14, wherein said cancer is selected from ovarian cancer, pancreatic cancer, prostate cancer, esophageal cancer, and melanoma.

21. The use of claim 14, wherein said cancer is ovarian cancer or pancreatic cancer.

22. The use of claim 14, wherein said relacorilant is to be administered orally.

23. The use of claim 14, wherein paclitaxel is in the form of nab-paclitaxel, and wherein relacorilant is to be administered intermittently the day before, the day of and the day after the nab-paclitaxel administration, at a dose selected from 75, mg, 100 mg, 150 mg, 175 mg, 200 mg, and 200 mg of relacorilant.

24. The use of claim 14, wherein the doses of relacorilant and of paclitaxel are to be administered according to a 28-day schedule, wherein paclitaxel is in the form of nab-paclitaxel, wherein the dose of nab-paclitaxel is selected from 60 mg/m^2, 72 mg/m^2, 75 mg/m^2, 80 mg/m^2, and 83 mg/m^2 of nab-paclitaxel to be administered by intravenous infusion on days 1, 8 and 15 of each 28-day cycle.