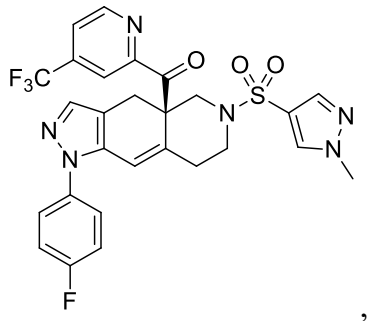
cancer. There is a large unmet need for effective, well-tolerated treatments for women with platinum-resistant ovarian cancer.

SUMMARY

[0008] Disclosed herein are novel methods for treating cancers, and novel uses of glucocorticoid receptor modulator (GRM) compounds, such as nonsteroidal GRMs, including heteroaryl-ketone fused azadecalin compounds, for treating cancers.

[0008a] In one aspect, there is provided the use of the glucocorticoid receptor modulator (GRM) (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone ("relacorilant"), which has the following structure:

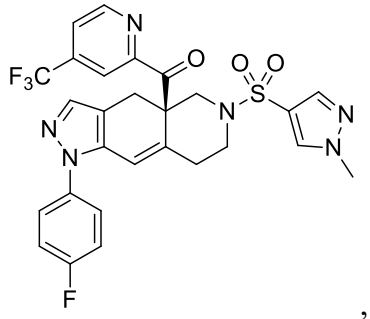


, in the manufacture of a medicament for treatment of cancer in a patient suffering from a cancerous tumor that expresses high levels of mRNA encoding the glucocorticoid receptor NR3C1,
wherein said patient previously suffered from progression of said cancerous tumor within six months after receiving a platinum-based cancer chemotherapy treatment,
wherein said cancerous tumor is selected from the group consisting of ovarian, fallopian tube, uterine, cervical, vaginal, vulvar, and peritoneal cancerous tumors, wherein:

an effective amount of the GRM is to be intermittently administered to a patient hosting said cancer, wherein said patient is in need of, and is receiving, taxane cancer chemotherapy treatment for said cancer, said treatment comprising a taxane cancer chemotherapy agent to be administered according to a monthly cancer chemotherapy dosing schedule, said dosing schedule requiring that relacorilant is to be administered to the patient once per day on days 1 and 2; once per day on days 7, 8, and 9; once per day on days 14, 15, and 16; and once again on day 28 during the monthly cycle in which said taxane cancer

chemotherapy agent is to be administered on days 1, 8, and 15 of the monthly cycle.

[0008b] In another aspect, there is provided the use of a pharmaceutical composition comprising a pharmaceutically acceptable excipient and the glucocorticoid-receptor modulator (GRM) R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone ("relacorilant"), which has the following structure:



, in the manufacture of a medicament for treatment of cancer in a patient suffering from a cancerous tumor that expresses high levels of mRNA encoding the glucocorticoid receptor NR3C1,
wherein said patient previously suffered from progression of said cancerous tumor within six months after receiving a platinum-based cancer chemotherapy treatment,
wherein said cancerous tumor is selected from the group consisting of ovarian, fallopian tube, uterine, cervical, vaginal, vulvar, and peritoneal cancerous tumors,
wherein said cancer treatment comprises an effective amount of the GRM to be intermittently administered to a patient hosting said cancer, wherein said patient is in need of, and is receiving, taxane cancer chemotherapy treatment for said cancer, said treatment comprising a taxane cancer chemotherapy agent to be administered according to a monthly cancer chemotherapy dosing schedule, said dosing schedule requiring relacorilant is to be administered to the patient once per day on days 1 and 2; once per day on days 7, 8, and 9; once per day on days 14, 15, and 16; and once again on day 28 during the monthly cycle in which said taxane cancer chemotherapy agent is to be administered on days 1, 8, and 15 of the monthly cycle.

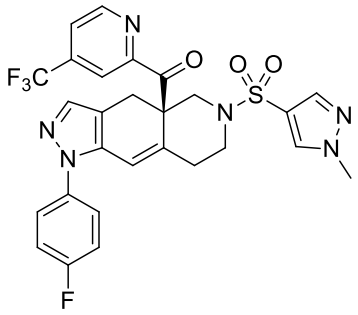
[0009] Applicant discloses methods of treating cancer which comprise intermittently administering a GRM to a cancer patient who is receiving cancer chemotherapy. The GRM may be administered orally. The methods include intermittently administering an effective amount of a GRM to a patient hosting a cancer, that patient being in need of, and receiving, cancer chemotherapy treatment for the cancer; the cancer chemotherapy treatment comprises administration of a cancer chemotherapy agent according to a cancer chemotherapy dosing schedule that includes at least one day without administration of the cancer chemotherapy agent between days of cancer chemotherapy agent administration. As disclosed herein, intermittent GRM administration comprises at least a first round of GRM administration and a second round of GRM administration, with at least one day without GRM administration separating the first round and the second round. The first round of GRM administration may be administration of a GRM on one day; or on two consecutive days; or on three consecutive days; or on more consecutive days. The second round of GRM administration may be administration of a GRM on one day; or on two consecutive days; or on three consecutive days; or on more consecutive days. The first round and the second round need not have the same number of days.

[0010] Intermittent GRM administration to a patient also receiving cancer chemotherapy may comprise administration of the GRM on days coordinated with the schedule of administration of the cancer chemotherapy. A round of GRM administration may be administered on a day related to, or may be administered on a day determined by, the cancer chemotherapy dosing schedule for the patient. For example, a round of GRM administration may be administered to the patient before, at the time of (e.g., on the same day as), or after the patient receives a dose of chemotherapy agent.

[0011] In examples, a round of GRM administration may be begun, or completed, one or more days before a day on which the patient is administered chemotherapy agent. In examples, a round of GRM administration may be begun, or completed, on a day on

WE CLAIM:

1. Use of the glucocorticoid receptor modulator (GRM) (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone ("relacorilant"), which has the following structure:



, in the manufacture of a medicament for treatment of cancer in a patient suffering from a cancerous tumor that expresses high levels of mRNA encoding the glucocorticoid receptor NR3C1,

wherein said patient previously suffered from progression of said cancerous tumor within six months after receiving a platinum-based cancer chemotherapy treatment,

wherein said cancerous tumor is selected from the group consisting of ovarian, fallopian tube, uterine, cervical, vaginal, vulvar, and peritoneal cancerous tumors, wherein:

an effective amount of the GRM is to be intermittently administered to a patient hosting said cancer, wherein said patient is in need of, and is receiving, taxane cancer chemotherapy treatment for said cancer, said treatment comprising a taxane cancer chemotherapy agent to be administered according to a monthly cancer chemotherapy dosing schedule, said dosing schedule requiring that relacorilant is to be administered to the patient once per day on days 1 and 2; once per day on days 7, 8, and 9; once per day on days 14, 15, and 16; and once again on day 28 during the monthly cycle in which said taxane cancer chemotherapy agent is to be administered on days 1, 8, and 15 of the monthly cycle.

2. The use of claim 1, wherein said cancer is ovarian cancer.

3. The use of claim 1, wherein the cancer chemotherapy agent is a taxane selected from the group of taxanes consisting of paclitaxel, nab-paclitaxel, docetaxel, larotaxel, tesetaxel, cabazitaxel, and ortataxel.

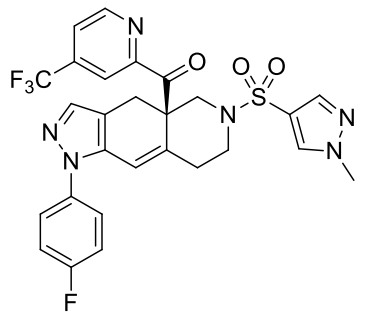
4. The use of claim 3, wherein the cancer chemotherapy agent is a taxane containing paclitaxel.

5. The use of claim 3, wherein the cancer chemotherapy agent is nab-paclitaxel.

6. The use of any of claims 1 to 5, wherein said cancer chemotherapy dosing schedule comprises said cancer chemotherapy agent to be administered on a first day, and again on a day seven days after said first day, without administration of said cancer chemotherapy agent on days between the first and said day seven days after said first day.

7. The use of any of claims 1 to 6, wherein the patient has been administered bevacizumab before receiving administration of said GRM.

8. Use of a pharmaceutical composition comprising a pharmaceutically acceptable excipient and the glucocorticoid-receptor modulator (GRM) (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone ("relacorilant"), which has the following structure:



, in the manufacture of a medicament for treatment of cancer in a patient suffering from a cancerous tumor that expresses high levels of mRNA encoding the glucocorticoid receptor NR3C1,

wherein said patient previously suffered from progression of said cancerous tumor within six months after receiving a platinum-based cancer chemotherapy treatment,

wherein said cancerous tumor is selected from the group consisting of ovarian, fallopian tube, uterine, cervical, vaginal, vulvar, and peritoneal cancerous tumors,

wherein said cancer treatment comprises an effective amount of the GRM to be intermittently administered to a patient hosting said cancer, wherein said patient is in need of, and is receiving, taxane cancer chemotherapy treatment for said cancer, said treatment comprising a taxane cancer chemotherapy agent to be administered according to a monthly cancer chemotherapy dosing schedule, said dosing schedule requiring relacorilant is to be administered to the patient once per day on days 1 and 2; once per day on days 7, 8, and 9; once per day on days 14, 15, and 16; and once again on day 28 during the monthly cycle in which said taxane cancer chemotherapy agent is to be administered on days 1, 8, and 15 of the monthly cycle.

9. The use of claim 8, wherein said cancer is ovarian cancer.

10. The use of claim 8, wherein the cancer chemotherapy agent is a taxane selected from the group of taxanes consisting of paclitaxel, nab-paclitaxel, docetaxel, larotaxel, tesetaxel, cabazitaxel, and ortataxel.

11. The use of claim 10, wherein the cancer chemotherapy agent is a taxane containing paclitaxel.

12. The use of claim 10, wherein the cancer chemotherapy agent is nab-paclitaxel.

13. The use of any of claims 8 to 12, wherein said cancer chemotherapy dosing schedule comprises said cancer chemotherapy agent to be administered on a first day, and again on a day seven days after said first day, without administration of said cancer chemotherapy agent on days between the first and said day seven days after said first day.

14. The use of any of claims 8 to 12, wherein the patient has received bevacizumab.