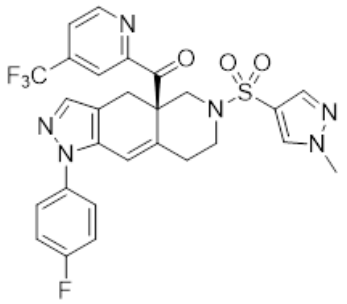
SUMMARY

[0007] Applicant discloses herein methods of normalizing neutrophil-to-lymphocyte ratio (NLR). For cancer patients, an NLR that is higher than normal (greater than 3) is predictive of poorer prognosis. Decreasing NLR has been correlated with improved cancer treatment outcomes. Reducing the NLR in cancer patients to a normal value (i.e., less than about 3) improves the prognoses of those patients, improves their response to cancer treatment, improves the outcomes of cancer therapies, can reduce tumor load and promote tumor elimination. As noted above, mifepristone does not alter neutrophil or lymphocyte abundance in healthy subjects, and so does not affect NLR in healthy subjects (Laue, 1990). Surprisingly, as disclosed herein, administration of a nonsteroidal GRA was effective to reduce NLR in cancer patients receiving cancer treatment.

[0008] The methods disclosed herein include selecting cancer patients who have an NLR of greater than 3 and administering a nonsteroidal glucocorticoid receptor antagonist (GRA) such as, e.g., relacorilant, in combination with a cancer treatment to normalize (reduce) NLR in cancer patients with high NLR and receiving cancer treatment. The methods disclosed herein include administering a nonsteroidal GRA such as, e.g., relacorilant, in combination with a cancer treatment to treat cancer patients with high NLR. The methods disclosed herein include administering a nonsteroidal GRA such as, e.g., relacorilant, in combination with a cancer treatment to enhance the response to cancer treatment in cancer patients with high NLR and receiving cancer treatment. The methods disclosed herein include administering a nonsteroidal GRA such as, e.g., relacorilant, in combination with a cancer treatment to reduce tumor load in cancer patients having a tumor or tumors and with high NLR and receiving cancer treatment. The methods disclosed herein include administering a nonsteroidal GRA such as, e.g., relacorilant, in combination with a cancer treatment to promote tumor elimination in cancer patients with high NLR and receiving cancer treatment. The methods disclosed herein include administering a nonsteroidal GRA such as, e.g., relacorilant, in combination with a cancer treatment to improve the health of cancer patients with high NLR. The methods disclosed herein include administering a nonsteroidal GRA such as, e.g., relacorilant, in combination with a taxane, such as nab-paclitaxel, to a cancer patient with high NLR to lower the NLR, to improve the response of the patient to the taxane, and to improve the health of the cancer patient.

[0008a] In one aspect of the present disclosure, there is provided a use of a nonsteroidal selective glucocorticoid receptor antagonist (GRA) (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, (also known as relacorilant), which has the structure:



,

in the manufacture of a medicament for reducing the neutrophil-to-lymphocyte ratio (NLR) by at least 25% in a cancer patient having a tumor and having a NLR greater than 3 prior to use of said GRA,

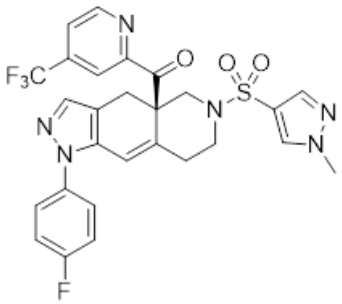
wherein an effective amount of the GRA is to be administered to said cancer patient,

whereby the NLR of said cancer patient is reduced by said at least 25% as compared to the NLR of the patient measured prior to use of the GRA.

[0009] In examples, the cancer treatment may include administration of a chemotherapeutic agent (e.g., a taxane, such as nab-paclitaxel, gemcitabine, or other

WE CLAIM:

1. Use of a nonsteroidal selective glucocorticoid receptor antagonist (GRA) (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, (also known as relacorilant), which has the structure:



,

in the manufacture of a medicament for reducing the neutrophil-to-lymphocyte ratio (NLR) by at least 25% in a cancer patient having a tumor and having a NLR greater than 3 prior to use of said GRA,

wherein an effective amount of the GRA is to be administered to said cancer patient,

whereby the NLR of said cancer patient is reduced by said at least 25% as compared to the NLR of the patient measured prior to use of the GRA.

2. The use of claim 1, wherein an effective amount of a cancer treatment and an effective amount of a nonsteroidal selective glucocorticoid receptor antagonist (GRA) is to be administered to said cancer patient,

whereby the NLR of said cancer patient is reduced by at least 25% as compared to the NLR of the patient measured prior to use of said GRA.

3. The use of claim 1 or claim 2, wherein said neutrophil-to-lymphocyte ratio (NLR) of said cancer patient is reduced to 3 or less.

4. The use of claim 2 or claim 3, wherein the use is effective to reduce the tumor load of the patient.

5. The use of any of claims 1 to 4, wherein said neutrophil-to-lymphocyte ratio (NLR) of said cancer patient is reduced to 3 or less.

6. The use of any of claims 2 to 4, wherein the cancer treatment comprises a chemotherapeutic agent or an immunotherapeutic agent.

7. The use of claim 6, wherein the chemotherapeutic agent is selected from the group consisting of antimicrotubule agents, alkylating agents, topoisomerase inhibitors, endoplasmic reticulum stress inducing agents, antimetabolites, mitotic inhibitors and combinations thereof, and

the immunotherapeutic agent comprises an antibody directed against a protein target selected from PD-1, PD-L1, CTKA4, LAG3, B7-H3, B7-H4, OX-40, CD137, and TIM3.

8. The use of claim 2, wherein the cancer treatment comprises one or more of cancer radiation therapy, growth factor inhibitors, and anti-angiogenesis factors.

9. The use of any of claims 2 to 8, wherein said reducing NLR is effective to enhance the response to cancer treatment in a cancer patient receiving cancer treatment and having a neutrophil-to-lymphocyte ratio of greater than 3, wherein said enhancing is as compared to the response in the absence of the present use, wherein the use comprises:

an effective amount of a cancer treatment and an effective amount of said GRA to be administered to said cancer patient,

whereby the cancer patient's NLR is reduced by at least 25% as compared to the NLR of the patient measured prior to use of said GRA and the cancer patient's response to cancer treatment is enhanced.

10. The use of claim 9, wherein the cancer treatment comprises a chemotherapeutic agent or an immunotherapeutic agent.

11. The use of claim 10, wherein the chemotherapeutic agent is selected from the group consisting of antimicrotubule agents, alkylating agents, topoisomerase inhibitors, endoplasmic reticulum stress inducing agents, antimetabolites, mitotic inhibitors and combinations thereof and the immunotherapeutic agent comprises an antibody directed against a protein target selected from PD-1, PD-L1, CTKA4, LAG3, B7-H3, B7-H4, OX-40, CD137, and TIM3.

12. The use of claim 9, wherein the cancer treatment comprises one or more of cancer radiation therapy, growth factor inhibitors, and anti-angiogenesis factors.

13. The use of any of claims 9 to 12, wherein the patient exhibits a partial response to the cancer treatment and GRA treatment, wherein said partial response is an improvement as compared to the patient's response to the cancer treatment alone,

whereby the cancer patient's NLR is reduced by at least 25% after 15 days of use of said GRA and a cancer treatment as compared to the patient's NLR prior to use of the GRA and the cancer patient's response to cancer treatment is enhanced.

14. The use of any of claims 9 to 12, wherein the patient exhibits a complete response to the cancer treatment and GRA treatment, wherein said complete response is an improvement as compared to the patient's response to the cancer treatment alone,

whereby the cancer patient's NLR is reduced by at least 25% after 15 days of use of said GRA and a cancer treatment as compared to the patient's NLR prior to use of the GRA and the cancer patient's response to cancer treatment is enhanced.