chemotherapy in killing cancer cells. See U.S. Pat. No. 9149485. This current invention uses a novel combination therapy that targets both the checkpoint signaling pathway and GR signaling pathway to treat patients suffering from a tumor load.

SUMMARY

[0005a] In one aspect of the present disclosure, there is provided a use of an antibody checkpoint inhibitor and a selective glucocorticoid receptor antagonist (SGRA), wherein the SGRA inhibits biological responses associated with the binding of a glucocorticoid (GR) to an agonist, wherein the tumor load is caused by a checkpoint inhibitor sensitive cancer that expresses the glucocorticoid receptor, wherein the antibody checkpoint inhibitor is selected from lambrolizumab, nivolumab, AMP-224, pidilizumab, ipilimumab, and tremelimumab, MEDI4736, MPDL3280A and BMS-936559 (MDX-1105), in the manufacture of a medicament for treating a patient hosting a tumor load, wherein the SGRA is CORT125134 ((R)-(1-(4-fluorophenyl)-6-((1-methyl-1Hpyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone), or is CORT125281 (((4aR,8aS)-1-(4-fluorophenyl)-6-((2-methyl-2H-1,2,3-triazol-4-yl)sulfonyl)-4,4a,5,6,7,8,8a,9-octahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone), and where the SGRA is to be administered to the patient in an amount effective to reduce the tumor load of the patient by at least 10% as compared to the tumor load reduction provided by said antibody checkpoint inhibitor alone.

[0006] The cancer treatment method disclosed herein includes administering to a patient suffering from a tumor load a therapeutic amount of a checkpoint inhibitor and a selective glucocorticoid receptor modulator (SGRM) in an amount effective to potentiate the activity of the checkpoint inhibitor. The combination therapy of the checkpoint inhibitor and SGRM provides superior tumor load reduction compared to treatment with a checkpoint inhibitor alone.

[0007] In some cases, the checkpoint inhibitor is an antibody against at least one checkpoint protein, e.g., PD-1, CTLA-4, PD-L1 or PD-L2. In some cases, the checkpoint inhibitor is an antibody that is effective against two or more of the checkpoint proteins selected from the group of PD-1, CTLA-4, PD-L1 and PD-L2.

WHAT IS CLAIMED IS:

1. Use of an antibody checkpoint inhibitor and a selective glucocorticoid receptor antagonist (SGRA), wherein the SGRA inhibits biological responses associated with the binding of a glucocorticoid (GR) to an agonist, wherein the tumor load is caused by a checkpoint inhibitor sensitive cancer that expresses the glucocorticoid receptor, wherein the antibody checkpoint inhibitor is selected from lambrolizumab, nivolumab, AMP-224, pidilizumab, ipilimumab, and tremelimumab in the manufacture of a medicament for treating a patient hosting a tumor load, wherein the SGRA is CORT125134 ((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), or is CORT125281 (((4aR,8aS)-1-(4-fluorophenyl)-6-((2-methyl-2H-1,2,3-triazol-4-yl)sulfonyl)-4,4a,5,6,7,8,8a,9-octahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridin-2-yl)methanone), and where the SGRA is to be administered to the patient in an amount effective to reduce the tumor load of the patient by at least 10% as compared to the tumor load reduction provided by said antibody checkpoint inhibitor alone.

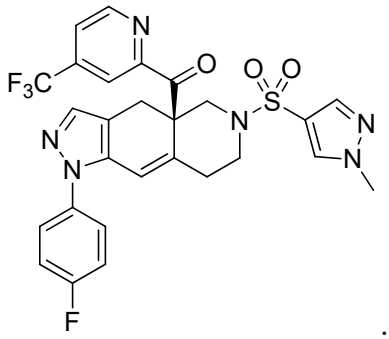
2. The use of claim 1, wherein the tumor load is due to the presence of a checkpoint inhibitor sensitive tumor.

3. The use of claim 1 wherein the checkpoint inhibitor is an antibody effective against PD-1.

4. The use of claim 1 wherein the checkpoint inhibitor is an antibody effective against CTLA-4.

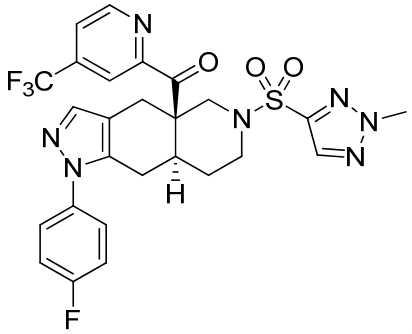
5. The use of claim 1 wherein the checkpoint inhibitor is an antibody effective against PD-L1 or PD-L2.

6. The use of claim 1 wherein the SGRA is CORT 125134



.

7. The use of claim 1, wherein the SGRA is CORT125281



.

8. The use of claim 1, wherein the tumor load is due to cancer, and wherein the cancer expresses the glucocorticoid receptor (GR^+).

9. The use of claim 8 wherein the cancer is a GR^+ cancer and wherein the cancer is selected from the group consisting of breast cancer, prostate cancer, Melanoma, Sarcoma, Renal cell cancer, Head and Neck cancer, Hepatocellular cancer, Glioblastoma, Cervical cancer, neuroendocrine cancer, Bladder cancer, Prostate cancer, Esophageal cancer, mesothelioma, Lung cancer, Ovarian cancer, Pancreas cancer, Gall bladder cancer, Gastric cancer, Endometrial cancer, and colon cancer.

10. The use of claim 1 wherein the SGRA is CORT125281 and the checkpoint inhibitor is an antibody effective against PD-1.

11. The use of claim 1 wherein the SGRA is CORT125134 and the checkpoint inhibitor is an antibody effective against PD-1.