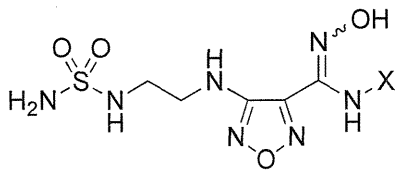
suppression of effector T-cell function and augmented differentiation of regulatory T cells (19-23). The anti-tumor efficacy of immunotherapeutic antibodies like anti-CTLA-4, anti-PD1/anti-PD-L1, and agonistic anti-GITR were significantly higher in IDO-deficient mice compared to wild type mice (24). This suggests that T-cell based immunotherapies were hampered due to IDO activity and blocking this pathway could boost the therapeutic potential of these antibodies.

[0006] INCB024360 is a selective inhibitor of IDO1 enzyme activity, which is currently in clinical development by Inctye Corporation as a single agent and in combination with other modalities for multiple cancers (25, 26).

[0007] MK-3475 is a selective humanized anti-human PD-1 monoclonal antibody of the IgG4/kappa isotype which is currently in clinical development by Merck as a single agent and in combination with other modalities for multiple cancers.

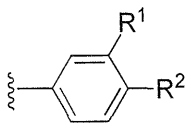
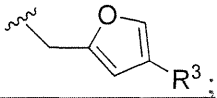
SUMMARY ~~OF THE INVENTION~~

[0008] In one embodiment, the ~~invention~~disclosure provides a method for treating a cancer in an individual comprising administering to the individual a combination therapy which comprises a PD-1 antagonist and an IDO1 inhibitor. In one aspect, there is provided use of an antagonist of a Programmed Death 1 protein (PD-1) in the manufacture of a medicament for treating a cancer in an individual, wherein the medicament is for use in a combination therapy with an inhibitor of indoleamine 2, 3-dioxygenase 1 (IDO1), wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

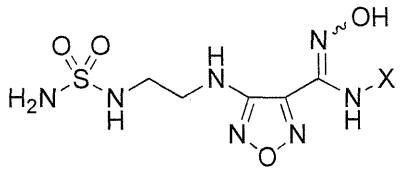
X is  or ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

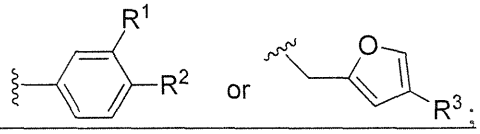
R^3 is Cl or Br.

[0009] In another embodiment, the ~~invention~~disclosure provides a medicament comprising a PD-1 antagonist for use in combination with an IDO1 inhibitor for treating a cancer. In another aspect, there is provided a medicament comprising an antagonist of a Programmed Death 1 protein (PD-1) for use in combination with a IDO1 inhibitor for treating a cancer in an individual, wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

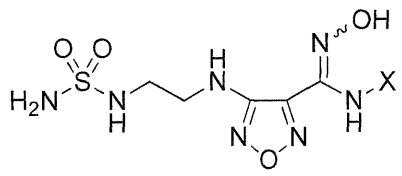
X is  ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

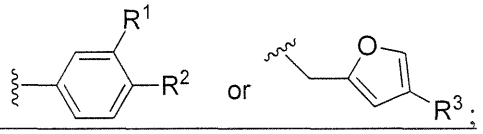
R^3 is Cl or Br.

[0010] In yet another embodiment, the ~~invention~~disclosure provides a medicament comprising a IDO1 inhibitor for use in combination with a PD-1 antagonist for treating a cancer. In another aspect, there is provided a medicament comprising a IDO1 inhibitor for use in combination with an antagonist of a Programmed Death 1 protein (PD-1) for treating a cancer in an individual, wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF_3, or CN;

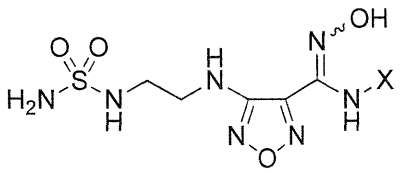
R^2 is H or F; and

R^3 is Cl or Br.

[0011] Other embodiments provide use of a PD-1 antagonist in the manufacture of medicament for treating a cancer in an individual when administered in combination with an IDO1 inhibitor and use of an IDO1 inhibitor in the manufacture of a medicament for treating a cancer in an individual when administered in combination with a PD-1 antagonist.

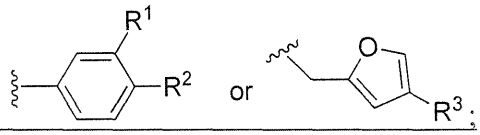
[0012] In a still further embodiment, the ~~invention~~disclosure provides use of a PD-1 antagonist and an IDO1 inhibitor in the manufacture of medicaments for treating a cancer in an individual. In some preferred embodiments, the medicaments comprise a kit, and the kit also comprises a package insert comprising instructions for using the PD-1 antagonist in combination with an IDO1 inhibitor to treat a cancer in an individual.

[0012a] In another aspect, there is provided a kit which comprises a first container, a second container and a package insert, wherein the first container comprises at least one dose of a medicament comprising an antagonist of a Programmed Death 1 protein (PD-1), the second container comprises at least one dose of a medicament comprising a IDO1 inhibitor, and the package insert comprises instructions for treating an individual for cancer using the medicaments, wherein the cancer is melanoma, bladder cancer, renal cell cancer, triple negative breast cancer, endometrial cancer or squamous cell carcinoma of the head and neck and wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  ;

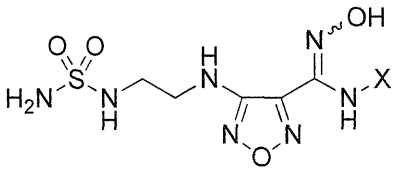
R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

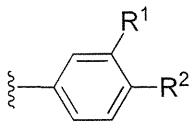
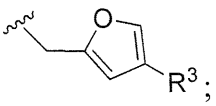
[0013] In all of the above treatment method, medicaments and uses, the PD-1 antagonist inhibits the binding of PD-L1 to PD-1, and preferably also inhibits the binding of PD-L2 to PD-1. In some preferred embodiments of the above treatment method, medicaments and uses, the PD-1 antagonist is a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to PD-1 or to PD-L1 and blocks the binding of PD-L1 to PD-1. In one particularly preferred embodiment, the PD-1 antagonist is an anti-PD-1 antibody which comprises a heavy chain and a light chain, and wherein the heavy and light chains comprise the amino acid sequences shown in Figure 6 (SEQ ID NO:21 and SEQ ID NO:22).

[0014] In all of the above embodiments of the treatment method, medicaments and uses, the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

[0015] In some embodiments of the above treatment method, medicaments and uses of the ~~invention~~disclosure, the individual is a human and the cancer is a solid tumor and in some preferred embodiments, the solid tumor is transitional cell cancer of the urinary bladder, adenocarcinoma of the endometrium, bladder cancer, breast cancer, clear cell kidney cancer, head/neck squamous cell carcinoma, lung squamous cell carcinoma, melanoma, non-small-cell lung cancer (NSCLC), ovarian cancer, pancreatic cancer, prostate cancer, renal cell cancer (RCC), small-cell lung cancer (SCLC) or triple negative breast cancer. In other preferred embodiments, the cancer is

advanced or metastatic NSCLC, melanoma, bladder cancer, renal cell cancer, triple negative breast cancer, endometrial cancer or squamous cell carcinoma of the head and neck, and in more preferred embodiments, the cancer is stage IIIb, stage IV or recurrent NSCLC in an individual previously treated with a platinum-based chemotherapy regimen.

[0016] In other embodiments of the above treatment method, medicaments and uses of the ~~invention~~disclosure, the individual is a human and the cancer is a Heme malignancy and in some preferred embodiments, the Heme malignancy is acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), diffuse large B-cell lymphoma (DLBCL), EBV-positive DLBCL, primary mediastinal large B-cell lymphoma, T-cell/histiocyte-rich large B-cell lymphoma, follicular lymphoma, Hodgkin's lymphoma (HL), mantle cell lymphoma (MCL), multiple myeloma (MM), myeloid cell leukemia-1 protein (Mcl-1), myelodysplastic syndrome (MDS), non-Hodgkin's lymphoma (NHL), or small lymphocytic lymphoma (SLL).

[0017] Also, in preferred embodiments of any of the above treatment method, medicaments and uses, the cancer tests positive for the expression of one or both of PD-L1 and PD-L2. In particularly preferred embodiments, the cancer has elevated PD-L1 expression.

[0018] In one particularly preferred embodiment of the above treatment method, medicaments and uses, the individual is a human and the cancer is advanced or metastatic NSCLC that tests positive for human PD-L1.

BRIEF DESCRIPTION OF THE DRAWINGS

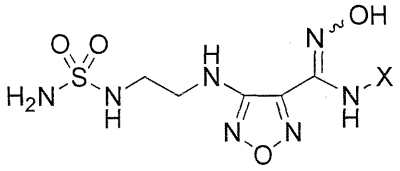
[0019] FIGURE 1 shows amino acid sequences of the light chain and heavy chain CDRs for an exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NOs:1-6).

[0020] FIGURE 2 shows amino acid sequences of the light chain and heavy chain CDRs for another exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NOs:7-12).

[0021] FIGURE 3 shows amino acid sequences of the heavy chain variable region and full length heavy chain for an exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NO:13 and SEQ ID NO:14).

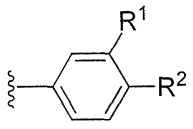
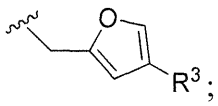
CLAIMS

1. Use of an antagonist of a Programmed Death 1 protein (PD-1) in the manufacture of a medicament for treating a cancer in an individual, wherein the medicament is for use in a combination therapy with an inhibitor of indoleamine 2, 3-dioxygenase 1 (IDO1), wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

2. The use according to claim 1, wherein the individual is a human and the PD-1 antagonist is

a) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-1 and blocks the binding of human PD-L1 to human PD-1; or

b) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-L1 and blocks the binding of human PD-L1 to human PD-1.

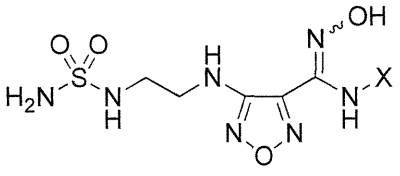
3. The use according to claim 2, wherein the PD-1 antagonist is an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, wherein the heavy and light chains comprise SEQ ID NO:21 and SEQ ID NO:22, respectively, or SEQ ID NO:23 and SEQ ID NO:24, respectively.

4. The use according to any one of claims 1 to 3, wherein the cancer is a solid tumor.

5. The use according to any one of claims 1 to 4, wherein the cancer or tumor is selected from non-small-cell lung cancer (NSCLC), melanoma, transitional cell cancer of the bladder (TCC), renal cell cancer (RCC), triple negative breast cancer, adenocarcinoma of the endometrium, or squamous cell carcinoma of the head and neck.

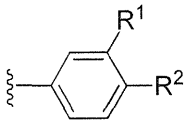
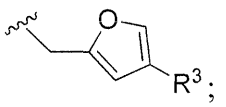
6. The use according to any one of claims 3 to 5, wherein the PD-1 antagonist is MK-3475.

7. A medicament comprising an antagonist of a Programmed Death 1 protein (PD-1) for use in combination with a IDO1 inhibitor for treating a cancer in an individual, wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

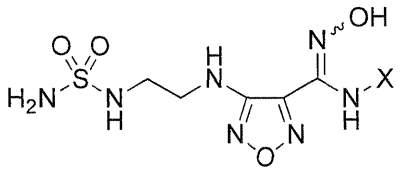
X is  or ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

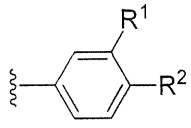
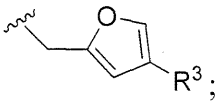
R^3 is Cl or Br.

8. A medicament comprising a IDO1 inhibitor for use in combination with an antagonist of a Programmed Death 1 protein (PD-1) for treating a cancer in an individual, wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

9. The medicament according to claim 7 or claim 8, wherein the individual is a human and the PD-1 antagonist is

a) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-1 and blocks the binding of human PD-L1 to human PD-1; or

b) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-L1 and blocks the binding of human PD-L1 to human PD-1.

10. The medicament according to any one of claims 7 to 9, wherein the PD-1 antagonist is an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, wherein the heavy and light chains comprise SEQ ID NO:21 and SEQ ID NO:22, respectively, or SEQ ID NO:23 and SEQ ID NO:24, respectively.

11. The medicament according to any one of claims 7 to 10, wherein the cancer is a solid tumor.

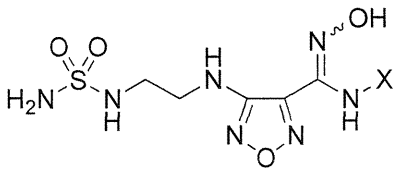
12. The medicament according to any one of claims 7 to 11, wherein the cancer is advanced renal cell carcinoma.

13. The medicament according to any one of claims 10 to 12, wherein the PD-1 antagonist is MK-3475 or nivolumab.

14. The medicament according to claim 13, wherein the MK-3475 is formulated as a liquid medicament which comprises 25 mg/ml MK-3475, 7% (w/v) sucrose, 0.02% (w/v) polysorbate 80 in 10 mM histidine buffer pH 5.5.

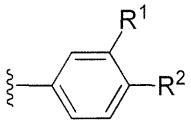
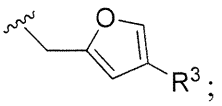
15. A kit which comprises a first container, a second container and a package insert, wherein the first container comprises at least one dose of a medicament comprising an antagonist of a Programmed Death 1 protein (PD-1), the second container comprises at least one dose of a medicament comprising a IDO1 inhibitor, and the package insert comprises

instructions for treating an individual for cancer using the medicaments, wherein the cancer is melanoma, bladder cancer, renal cell cancer, triple negative breast cancer, endometrial cancer or squamous cell carcinoma of the head and neck and wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF_3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

16. The kit according to claim 15, wherein the instructions state that the medicaments are intended for use in treating an individual having a cancer that tests positive for PD-L1 expression by an immunohistochemical (IHC) assay.

17. The kit according to claim 15 or claim 16, wherein the individual is a human and the PD-1 antagonist is

a) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-1 and blocks the binding of human PD-L1 to human PD-1; or

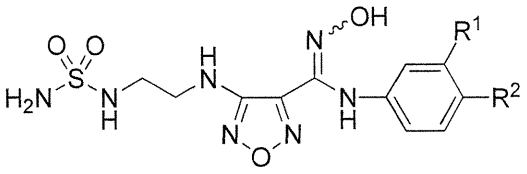
b) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-L1 and blocks the binding of human PD-L1 to human PD-1.

18. The kit according to any one of claims 15-17, wherein the PD-1 antagonist is MK-3475.

19. The use, medicament, or kit according to any one of claims 1 to 18, wherein the cancer is bladder cancer, breast cancer, clear cell kidney cancer, head/neck squamous cell carcinoma, lung squamous cell carcinoma, malignant melanoma, non-small-cell lung cancer

(NSCLC), ovarian cancer, pancreatic cancer, prostate cancer, renal cell cancer, small-cell lung cancer (SCLC), triple negative breast cancer, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, Hodgkin's lymphoma (HL), mantle cell lymphoma (MCL), multiple myeloma (MM), myeloid cell leukemia-1 protein (Mcl-1), myelodysplastic syndrome (MDS), non-Hodgkin's lymphoma (NHL), or small lymphocytic lymphoma (SLL).

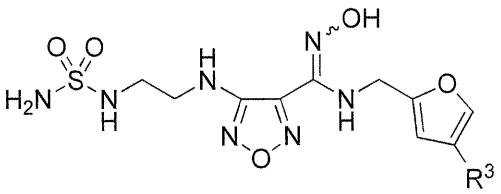
20. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is a compound of Formula Ia:



Ia

or a pharmaceutically acceptable salt thereof.

21. The use, medicament, or kit of any one of claims 1 to 19, wherein the IDO inhibitor is a compound of Formula Ib:



Ib

or a pharmaceutically acceptable salt thereof.

22. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

23. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-(3-chloro-4-fluorophenyl)-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

24. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-[4-fluoro-3-

(trifluoromethyl)phenyl]-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

25. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N'-hydroxy-N-[3-(trifluoromethyl)phenyl]-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

26. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-(3-cyano-4-fluorophenyl)-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

27. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-[(4-bromo-2-furyl)methyl]-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

28. The use, medicament, or kit according to any one of claims 1 to 19, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-[(4-chloro-2-furyl)methyl]-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

29. The use, medicament, or kit according to any one of claims 1 to 19, wherein the PD-1 antagonist is MK-3475 and the IDO inhibitor is INCB024360.

30. The use, medicament, or kit according to claim 29, wherein the PD-1 antagonist is to be administered to a subject in need in an amount of 2 mg/kg and the IDO inhibitor is to be administered to the subject at a dose of 25 mg or 50 mg.

31. The use, medicament, or kit according to claim 29, wherein the PD-1 antagonist is to be administered to a subject in need in an amount of 200 mg and the IDO inhibitor is to be administered to the subject at a dose of 25 mg or 50 mg.

32. The use, medicament, or kit according to claim 30, wherein the PD-1 antagonist is to be administered to a subject in need in an amount of 2 mg/kg and the IDO inhibitor is to be administered to the subject at a dose of 25 mg.

33. The use, medicament, or kit according to claim 30, wherein the PD-1 antagonist is to be administered to a subject in need in an amount of 2 mg/kg and the IDO inhibitor is to be administered to the subject at a dose of 50 mg.

34. The use, medicament, or kit according to claim 31, wherein the PD-1 antagonist is to be administered to a subject in need in an amount of 200 mg and the IDO inhibitor is to be administered to the subject at a dose of 25 mg.

35. The use, medicament, or kit according to claim 31, wherein the PD-1 antagonist is to be administered to a subject in need in an amount of 200 mg and the IDO inhibitor is to be administered to the subject at a dose of 50 mg.

36. The use, medicament, or kit according to any one of claims 30 to 35, wherein the IDO inhibitor is to be administered to the subject at a dose of 25 mg BID.

37. The use, medicament, or kit according to any one of claims 30 to 35, wherein the IDO inhibitor is to be administered to the subject at a dose of 50 mg BID.

38. The use, medicament, or kit according to any one of claims 30 to 37, wherein the PD-1 antagonist is to be administered every three weeks and one dose of the IDO inhibitor is to be administered two times per day.

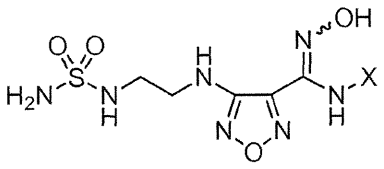
39. The use, medicament, or kit according to claim 38, wherein the IDO inhibitor is to be administered at twelve hour intervals.

40. The use, medicament, or kit according to any one of claims 30 to 39, wherein the PD-1 antagonist and the IDO inhibitor are dosed over a 21-day dosing period.

41. The use, medicament, or kit according to any one of claims 30 to 40, wherein the cancer is selected from one or more of non-small-cell lung cancer (NSCLC), melanoma, transitional cell cancer of the bladder (TCC), renal cell cancer (RCC), triple negative breast cancer, adenocarcinoma of the endometrium, or squamous cell carcinoma of the head and neck.

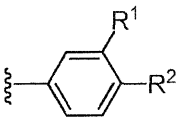
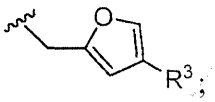
CLAIMS

1. A method for treating a cancer in an individual comprising administering to the individual a combination therapy which comprises an antagonist of a Programmed Death 1 protein (PD-1) and an inhibitor of indoleamine 2, 3-dioxygenase 1 (IDO1), wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

2. The method according to claim 1, wherein the individual is a human and the PD-1 antagonist is

a) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-1 and blocks the binding of human PD-L1 to human PD-1; or

b) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-L1 and blocks the binding of human PD-L1 to human PD-1.

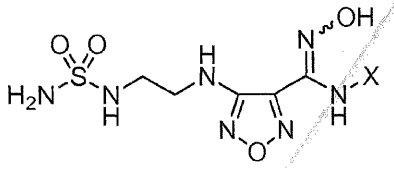
3. The method according to claim 2, wherein the PD-1 antagonist is an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, wherein the heavy and light chains comprise SEQ ID NO:21 and SEQ ID NO:22, respectively, or SEQ ID NO:23 and SEQ ID NO:24, respectively.

4. The method according to any one of claims 1 to 3, wherein the cancer is a solid tumor.

5. The method according to any one of claims 1 to 4, wherein the cancer or tumor is selected from non-small-cell lung cancer (NSCLC), melanoma, transitional cell cancer of the bladder (TCC), renal cell cancer (RCC), triple negative breast cancer, adenocarcinoma of the endometrium, or squamous cell carcinoma of the head and neck.

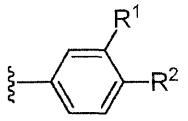
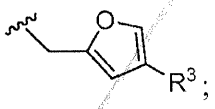
6. The method according to any one of claims 3 to 5, wherein the PD-1 antagonist is MK-3475.

7. A medicament comprising an antagonist of a Programmed Death 1 protein (PD-1) for use in combination with a IDO1 inhibitor for treating a cancer in an individual, wherein the wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

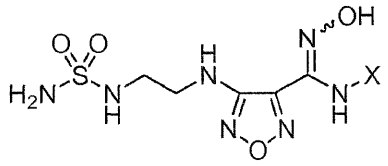
X is  or ;

R^1 is Cl, Br, CF3, or CN;

R^2 is H or F; and

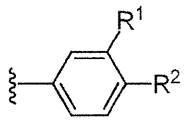
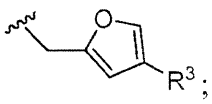
R^3 is Cl or Br.

8. A medicament comprising a IDO1 inhibitor for use in combination with an antagonist of a Programmed Death 1 protein (PD-1) for treating a cancer in an individual, wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

9. The medicament according to claim 7 or claim 8, wherein the individual is a human and the PD-1 antagonist is

a) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-1 and blocks the binding of human PD-L1 to human PD-1; or

b) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-L1 and blocks the binding of human PD-L1 to human PD-1.

10. The medicament according to any one of claims 7 to 9, wherein the PD-1 antagonist is an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, wherein the heavy and light chains comprise SEQ ID NO:21 and SEQ ID NO:22, respectively, or SEQ ID NO:23 and SEQ ID NO:24, respectively.

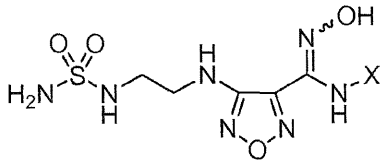
11. The medicament according to any one of claims 7 to 10, wherein the cancer is a solid tumor.

12. The medicament according to any one of claims 7 to 11, wherein the cancer is advanced renal cell carcinoma.

13. The medicament according to any one of claims 10 to 12, wherein the PD-1 antagonist is MK-3475 or nivolumab.

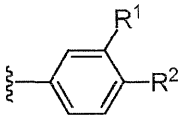
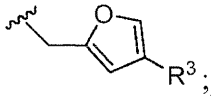
14. The medicament according to claim 13, wherein the MK-3475 is formulated as a liquid medicament which comprises 25 mg/ml MK-3475, 7% (w/v) sucrose, 0.02% (w/v) polysorbate 80 in 10 mM histidine buffer pH 5.5.

15. A kit which comprises a first container, a second container and a package insert, wherein the first container comprises at least one dose of a medicament comprising an antagonist of a Programmed Death 1 protein (PD-1), the second container comprises at least one dose of a medicament comprising a IDO1 inhibitor, and the package insert comprises instructions for treating an individual for cancer using the medicaments, wherein the cancer is melanoma, bladder cancer, renal cell cancer, triple negative breast cancer, endometrial cancer or squamous cell carcinoma of the head and neck and wherein the IDO1 inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof; wherein:

X is  or ;

R^1 is Cl, Br, CF3, or CN;

R^2 is H or F; and

R^3 is Cl or Br.

16. The kit according to claim 16, wherein the instructions state that the medicaments are intended for use in treating an individual having a cancer that tests positive for PD-L1 expression by an immunohistochemical (IHC) assay.

17. The kit according to claim 16 or claim 17, wherein the individual is a human and the PD-1 antagonist is

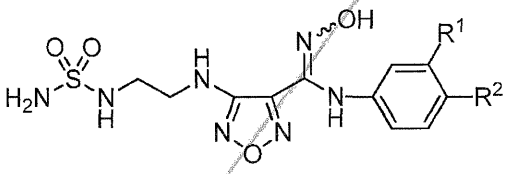
a) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-1 and blocks the binding of human PD-L1 to human PD-1; or

b) a monoclonal antibody, or an antigen binding fragment thereof, which specifically binds to human PD-L1 and blocks the binding of human PD-L1 to human PD-1.

18. The kit according to any one of claims 16-18, wherein the PD-1 antagonist is MK-3475.

19. The method, use or kit according to any one of claims 1 to 19, wherein the cancer is bladder cancer, breast cancer, clear cell kidney cancer, head/neck squamous cell carcinoma, lung squamous cell carcinoma, malignant melanoma, non-small-cell lung cancer (NSCLC), ovarian cancer, pancreatic cancer, prostate cancer, renal cell cancer, small-cell lung cancer (SCLC), triple negative breast cancer, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, Hodgkin's lymphoma (HL), mantle cell lymphoma (MCL), multiple myeloma (MM), myeloid cell leukemia-1 protein (Mcl-1), myelodysplastic syndrome (MDS), non-Hodgkin's lymphoma (NHL), or small lymphocytic lymphoma (SLL).

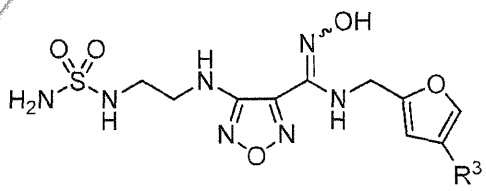
20. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is a compound of Formula Ia:



Ia

or a pharmaceutically acceptable salt thereof.

21. The method, medicament, or kit of any one of claims 1 to 20, wherein the IDO inhibitor is a compound of Formula Ib:



Ib

or a pharmaceutically acceptable salt thereof.

22. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

23. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-(3-chloro-4-fluorophenyl)-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

24. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

25. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N'-hydroxy-N-[3-(trifluoromethyl)phenyl]-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

26. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-(3-cyano-4-fluorophenyl)-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

27. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-[(4-bromo-2-furyl)methyl]-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

28. The method, medicament, or kit according to any one of claims 1 to 20, wherein the IDO inhibitor is 4-({2-[(aminosulfonyl)amino]ethyl}amino)-N-[(4-chloro-2-furyl)methyl]-N'-hydroxy-1,2,5-oxadiazole-3-carboximidamide, or a pharmaceutically acceptable salt thereof.

29. The method, medicament, or kit according to any one of claims 1 to 20, wherein the PD-1 antagonist is MK-3475 and the IDO inhibitor is INCB024360.

30. The method, medicament, or kit according to claim 29, wherein the PD-1 antagonist is administered to a subject in need in an amount of 2 mg/kg and the IDO inhibitor is administered to the subject at a dose of 25 mg or 50 mg.

31. The method, medicament, or kit according to claim 29, wherein the PD-1 antagonist is administered to a subject in need in an amount of 200 mg and the IDO inhibitor is administered to the subject at a dose of 25 mg or 50 mg.

32. The method, medicament, or kit according to claim 30, wherein the PD-1 antagonist is administered to a subject in need in an amount of 2 mg/kg and the IDO inhibitor is administered to the subject at a dose of 25 mg.

33. The method, medicament, or kit according to claim 30, wherein the PD-1 antagonist is administered to a subject in need in an amount of 2 mg/kg and the IDO inhibitor is administered to the subject at a dose of 50 mg.

34. The method, medicament, or kit according to claim 31, wherein the PD-1 antagonist is administered to a subject in need in an amount of 200 mg and the IDO inhibitor is administered to the subject at a dose of 25 mg.

35. The method, medicament, or kit according to claim 31, wherein the PD-1 antagonist is administered to a subject in need in an amount of 200 mg and the IDO inhibitor is administered to the subject at a dose of 50 mg.

36. The method, medicament, or kit according to any one of claims 30 to 35, wherein the IDO inhibitor is administered to the subject at a dose of 25 mg BID.

37. The method, medicament, or kit according to any one of claims 30 to 35, wherein the IDO inhibitor is administered to the subject at a dose of 50 mg BID.

38. The method, medicament, or kit according to any one of claims 30 to 37, wherein the PD-1 antagonist is administered every three weeks and one dose of the IDO inhibitor is administered two times per day.

39. The method, medicament, or kit according to claim 38, wherein the IDO inhibitor is administered at twelve hour intervals.

40. The method, medicament, or kit according to any one of claims 30 to 39, wherein the PD-1 antagonist and the IDO inhibitor are dosed over a 21-day dosing period.

41. The method, medicament, or kit according to any one of claims 30 to 40, wherein the cancer is selected from one or more of non-small-cell lung cancer (NSCLC), melanoma, transitional cell cancer of the bladder (TCC), renal cell cancer (RCC), triple negative breast cancer, adenocarcinoma of the endometrium, or squamous cell carcinoma of the head and neck.