[0009] In some examples, the present disclosure provides a method for treating a cancer in a subject in need thereof comprising administering to the subject: a first immune checkpoint polypeptide or a polynucleotide encoding the same; a second immune checkpoint polypeptide or a polynucleotide encoding the same; and an immune checkpoint inhibitor.

[0010] In some examples, the present disclosure provides a method of preventing disease progression in a subject suffering from a cancer comprising administering to the subject: a first immune checkpoint polypeptide or a polynucleotide encoding the same; a second immune checkpoint polypeptide or a polynucleotide encoding the same; and an immune checkpoint inhibitor.

[0011] In some examples, the present disclosure provides a method of reducing tumor volume in a subject suffering from a cancer comprising administering to the subject: a first immune checkpoint polypeptide or a polynucleotide encoding the same; a second immune checkpoint polypeptide or a polynucleotide encoding the same; and an immune checkpoint inhibitor.

[0012] In some examples, the subject has not previously received treatment with the immune checkpoint inhibitor. In some examples, the subject has previously received treatment with the immune checkpoint inhibitor. In some examples, the subject was refractory to the treatment with the immune checkpoint inhibitor or developed resistance to the immune checkpoint inhibitor during the course of the previous treatment.

[0013] In some examples, the first and second immune checkpoint polypeptide are independently selected from an IDO1 peptide, a PD-1 peptide, a PD-L1 peptide, a PD-L2 peptide, a CTLA4 peptide, a B7-H3 peptide, a B7-H4 peptide, an HVEM peptide, a BTLA peptide, a GAL9 peptide, a TIM3 peptide, a LAG3 peptide, or a KIR polypeptide.

[0014] In some examples, the first immune checkpoint polypeptide is an IDO1 polypeptide and wherein the second immune checkpoint polypeptide is a PD-L1 polypeptide. In some examples, the IDO1 polypeptide consists of up to 50 consecutive amino acids of SEQ ID NO: 1, and wherein said consecutive amino acids comprise the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3). In some examples, the IDO1 polypeptide comprises or consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3). In some examples, the

PD-L1 polypeptide consists of up to 50 consecutive amino acids of SEQ ID NO: 14, and wherein said consecutive amino acids comprise the sequence of any one of SEQ ID NOs: 15 to 32. In some examples, the PD-L1 polypeptide consists of up to 50 consecutive amino acids of SEQ ID NO: 14, and wherein said consecutive amino acids comprise the sequence of any one of SEQ ID NOs: 15, 25, 28 or 32. In some examples, the PD-L1 peptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32).

[0015] In some examples, the IDO1 polypeptide comprises or consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3) and the PD-L1 peptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32).

[0016] In some examples, the immune checkpoint inhibitor is an antibody or small molecule inhibitor (SMI). In some examples, the SMI is an inhibitor of IDO1. In some examples, the SMI is selected from Epacadostat (INCB24360), Indoximod, GDC-0919 (NLG919), and F001287. In some examples, the antibody binds to CTLA4 or PD1. In some examples, the antibody that binds to CTLA4 is ipilimumab. In some examples, the antibody that binds to PD-1 is pembrolizumab or nivolumab.

[0017] In some examples, the first and second immune checkpoint polypeptides or polynucleotides encoding the same are administered as a first composition and the immune checkpoint inhibitor is administered as a second composition. In some examples, the first and second immune checkpoint polypeptides or polynucleotides encoding the same and the immune checkpoint inhibitor are administered as one composition.

[0018] In some examples, the compositions further comprise an adjuvant or carrier. In some examples, the adjuvant is selected from herein said adjuvant is a Montanide ISA adjuvant, a bacterial DNA adjuvant, an oil/surfactant adjuvant, a viral dsRNA adjuvant, an imidazoquinoline, and GM-CSF. In some examples, the Montanide ISA adjuvant is selected from Montanide ISA 51 and Montanide ISA 720.

[0019] In some examples, the disease does not progress for at least 12 months, at least 2 years, at least 3 years, at least 4 years, at least 5 years, or longer after completion of treatment.

[0020] In some examples, the cancer is selected from prostate cancer, brain cancer, breast cancer, colorectal cancer, pancreatic cancer, ovarian cancer, lung cancer, cervical cancer, liver cancer, head/neck/throat cancer, skin cancer, bladder cancer, or a hematologic cancer. In some examples, the cancer is a solid tumor cancer selected from an adenoma, an adenocarcinoma, a blastoma, a carcinoma, a desmoid tumour, a desmopolastic small round cell tumour, an endocrine tumour, a germ cell tumour, a lymphoma, a leukaemia, a sarcoma, a Wilms tumour, a lung tumour, a colon tumour, a lymph tumour, a breast tumour, or a melanoma. In some examples, the cancer is metastatic melanoma.

[0021] In some examples, the subject has an immune profile indicative of response to treatment with the first immune checkpoint polypeptide or the polynucleotide encoding the same, the second immune checkpoint polypeptide or the polynucleotide encoding the same, and the immune checkpoint inhibitor.

[0022] In some examples, the present disclosure provides a method for treating a cancer in a subject in need thereof comprising administering to the subject: an IDO immune checkpoint polypeptide or a polynucleotide encoding the same, wherein the IDO polypeptide comprises or consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3); a PD-L1 immune checkpoint polypeptide or a polynucleotide encoding the same, wherein the PD-L1 polypeptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32); and an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is an anti-PD1 antibody.

[0023] In some examples, the present disclosure provides a method of preventing disease progression in a subject suffering from a cancer comprising administering to the subject: an IDO immune checkpoint polypeptide or a polynucleotide encoding the same, wherein the IDO polypeptide comprises or consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3); a PD-L1immune checkpoint polypeptide or a polynucleotide encoding the same, wherein the PD-L1 polypeptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32); and an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is an anti-PD1 antibody.

[0024] In some examples, the present disclosure provides a method of reducing tumor volume in a subject suffering from a cancer comprising administering to the subject: an IDO immune checkpoint polypeptide or a polynucleotide encoding the same, wherein the IDO polypeptide comprises or consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3); a PD-L1 immune checkpoint polypeptide or a polynucleotide encoding the same, wherein the PD-L1 polypeptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32); and an immune checkpoint inhibitor, wherein the immune checkpoint inhibitor is an anti-PD1 antibody.

[0025] In some examples, the subject has an immune profile indicative of response to treatment with the IDO polypeptide or polynucleotide encoding the same, the PD-L1 polypeptide or polynucleotide encoding the same, and the anti-PD1 antibody.

[0026] In some examples, the present disclosure provides a kit comprising: a first immune checkpoint polypeptide or a polynucleotide encoding the same; a second immune checkpoint polypeptide or a polynucleotide encoding the same; and an immune checkpoint inhibitor.

[0027] In some examples, first and second immune checkpoint polypeptides or polynucleotides encoding the same are provided as a single composition, in a separate sealed container from immune checkpoint inhibitor.

[0028] In some examples, the present disclosure provides an immunotherapeutic composition for use in a method for the prevention or treatment of cancer in a subject, wherein the immunotherapeutic composition comprises a first immune checkpoint polypeptide or a polynucleotide encoding the same and a second immune checkpoint polypeptide or a polynucleotide encoding the same.

[0029] In some examples, the present disclosure provides use of an immunotherapeutic composition in the manufacture of a medicament for the prevention or treatment of cancer in a subject, the immunotherapeutic composition comprising a first immune checkpoint polypeptide or a polynucleotide encoding the same and a second immune checkpoint polypeptide or a polynucleotide encoding the same, which is formulated for administration before, concurrently with, and/or after an immune checkpoint inhibitor.

[0030] In some examples, the subject has an immune profile indicative of response to treatment with the first immune checkpoint polypeptide or the polynucleotide encoding the same, the second immune checkpoint polypeptide or the polynucleotide encoding the same, and the immune checkpoint inhibitor. In some examples, wherein the first immune polypeptide is an IDO1 polypeptide, the second immune polypeptide is a PD-L1 polypeptide and the immune checkpoint inhibitor is an antibody that binds to PD1.

[0031] In some examples, the immune profile comprises one or more of the following: a decrease in CD4+ T regulatory cells compared to a control subject group; a decrease in CD28+CD4+ T cells compared to a control subject group; an increase in LAG-3+ CD4+ T cells compared to a control subject group; a decrease in monocytic-myeloid derived suppressor cells (mMDSCs) compared to a control subject group; an increase in CD56dimCD16+ Natural Killer (NK) cells compared to a control subject group; a decrease in CD56brightCD16- NK cells compared to a control subject group; and/or an increase in conventional dendritic cells type 2 (cDC2) compared to a control subject group.

[0032] In some examples, the cell populations are determined by FACS analysis of a peripheral blood sample obtained from the subject.

[0033] In some examples, the present disclosure provides a method for stratifying a cancer patient into one of at least two treatment groups, wherein said method comprises analysing one or more cell populations in a peripheral blood sample from the patient to determine an immune profile; and: i. stratifying the patient into a first treatment group if the immune profile determined is indicative of response to treatment with an IDO1 polypeptide, a PD-L1 polypeptide and an antibody that binds to PD1; or ii. stratifying the patient into a second treatment group if the immune profile determined in step indicates that the subject will not respond to said treatment.

[0034] In some examples, the first treatment group is to be treated, or is treated with, the IDO1 polypeptide, the PD-L1 polypeptide and the antibody that binds to PD1 and the second treatment group is to be treated with, or is treated with, one or more alternative therapies. In some examples, the immune profile is a baseline immune profile.

[0035] In some examples, the immune profile indicative of response to treatment comprises or more of: a) a decrease in CD4+ T regulatory cells compared to a control subject population; b) a decrease in CD28+CD4+ T cells compared to a control

subject population; c) an increase in LAG-3+ CD4+ T cells compared to a control subject population; d) a decrease in monocytic-myeloid derived suppressor cells (mMDSCs), compared to a control subject population; e) an increase in $CD56^{dim}CD16+$ Natural Killer (NK) cells compared to a control subject population; f) a decrease in $CD56^{bright}CD16-$ Natural Killer (NK) cells compared to a control subject population; and g) an increase in conventional dendritic cells type 2 (cDC2) compared to a control subject population.

[0036] In some examples, the present disclosure provides a method of monitoring the response of a cancer patient to treatment with an IDO1 polypeptide, a PD-L1 polypeptide and an antibody that binds to PD1, wherein said method comprises analysing one or more cell populations in a peripheral blood sample from the patient to determine an immune profile, and: i. determining that the patient is responding to treatment if the patient has an immune profile indicative of response to treatment; or ii. determining that the patient is not responding to treatment if the patient does not have an immune profile indicative of response to treatment.

[0037] In some examples, the immune profile indicative of response to treatment comprises increased expression of CD28, HLA-DR, CD39, TIGIT and/or TIM-3 on CD4+ T cells and/or increased expression of HLA-DR, CD39, LAG-3 and/or TIGIT on CD8+ T-cells.

[0038] In some examples, the cancer patient has a metastatic melanoma.

[0038a] In one aspect, the present disclosure relates to use of an immunotherapeutic composition in the manufacture of a medicament for treating or preventing a cancer in a subject in need thereof, or preventing disease progression or reducing tumor volume in a subject suffering from a cancer, wherein the immunotherapeutic composition comprises : a) a first immune checkpoint polypeptide or a polynucleotide encoding the same; b) a second immune checkpoint polypeptide or a polynucleotide encoding the same; and c) an immune checkpoint inhibitor.

[0038b] In another aspect, the present disclosure relates to a kit comprising: a) a first immune checkpoint polypeptide or a polynucleotide encoding the same; b) a second immune checkpoint polypeptide or a polynucleotide encoding the same; and c) an immune checkpoint inhibitor.

[0038c] In another aspect, the present disclosure relates to use of an immunotherapeutic composition in the manufacture of a medicament for the prevention or treatment of cancer in a subject, the immunotherapeutic composition comprising a) a first immune checkpoint polypeptide or a polynucleotide encoding the same and/or b) a second immune checkpoint polypeptide or a polynucleotide encoding the same as disclosed herein, which is formulated for administration before, concurrently with, and/or after an immune checkpoint inhibitor.

[0038d] In another aspect, the present disclosure relates to a method for stratifying a cancer patient into one of at least two treatment groups, wherein said method comprises analysing one or more cell populations in a peripheral blood sample from the patient to determine an immune profile; and: i. stratifying the patient into a first treatment group if the immune profile determined is indicative of response to treatment with an IDO1 polypeptide, a PD-L1 polypeptide and an antibody that binds to PD1; or ii. stratifying the patient into a second treatment group if the immune profile determined in step i. indicates that the subject will not respond to said treatment, optionally wherein the first treatment group is to be treated, or is treated with, the IDO1 polypeptide, the PD-L1 polypeptide and the antibody that binds to PD1 and the second treatment group is to be treated with, or is treated with, one or more alternative therapies, and/or wherein the immune profile is a baseline immune profile.

[0038e] In another aspect, the present disclosure relates to a method of monitoring the response of a cancer patient to treatment with an IDO1 polypeptide, a PD-L1 polypeptide and an antibody that binds to PD1, wherein said method comprises analysing one or more cell populations in a peripheral blood sample from the patient to determine an immune profile, and: i. determining that the patient is responding to treatment if the patient has an immune profile indicative of response to treatment; or ii. determining that the patient is not responding to treatment if the patient does not have an immune profile indicative of response to treatment.

BRIEF DESCRIPTION OF THE FIGURES

[0039] Fig. 1A – Fig. 1B provide schematics describing the methods provided herein. Fig. 1A illustrates the hypothesized mechanism of action for the combination immunotherapy regimen described herein (*e.g.*, IDO/PD-L1 peptide vaccine and nivolumab (anti-PD1)). Fig. 1B provides a schematic of the combination immunotherapy regimen described herein.

[0040] Fig. 2A – Fig. 2F show various clinical responses. Fig. 2A provides percentages of overall response rate (ORR), complete response (CR), partial response (PR), and progressive disease (PD) according to RECIST 1.1 by investigator review in all patients (n=30). Fig. 2B illustrates treatment effect in MM1636 compared with a matched historical control group from the DAMMED database (n=74). Fig. 2C provides the best change in the sum of target lesion compared with baseline (n=30). Fig. 2D provides Kaplan-Meier curve of duration of response in the 24 patients with an objective response.

CLAIMS

1. Use of an immunotherapeutic composition in the manufacture of a medicament for treating or preventing a cancer in a subject in need thereof, or preventing disease progression or reducing tumor volume in a subject suffering from a cancer, wherein the immunotherapeutic composition comprises :

a) a first immune checkpoint polypeptide or a polynucleotide encoding the same;
b) a second immune checkpoint polypeptide or a polynucleotide encoding the same; and
c) an immune checkpoint inhibitor.

2. The use according to claim 1, wherein the subject has not previously received treatment with the immune checkpoint inhibitor or wherein the subject has previously received treatment with the immune checkpoint inhibitor, optionally wherein the subject was refractory to the treatment with the immune checkpoint inhibitor or developed resistance to the immune checkpoint inhibitor during the course of the previous treatment.

3. The use according to claim 1 or 2, wherein the first and second immune checkpoint polypeptide are independently selected from an IDO1 polypeptide, a PD-1 polypeptide, a PD-L1 polypeptide, a PD-L2 polypeptide, a CTLA4 polypeptide, a B7-H3 polypeptide, a B7-H4 polypeptide, an HVEM polypeptide, a BTLA polypeptide, a GAL9 polypeptide, a TIM3 polypeptide, a LAG3 polypeptide, or a KIR polypeptide.

4. The use according to any one of claims 1-3, wherein the first immune checkpoint polypeptide is an IDO1 polypeptide and wherein the second immune checkpoint polypeptide is a PD-L1 polypeptide, optionally wherein

(i) the IDO1 polypeptide consists of up to 50 consecutive amino acids of SEQ ID NO: 1, and wherein said consecutive amino acids comprise the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3), and/or wherein the IDO1 polypeptide consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3); or

(ii) the PD-L1 polypeptide consists of up to 50 consecutive amino acids of SEQ ID NO: 14, and wherein said consecutive amino acids comprise the sequence of any one of SEQ ID NOs: 15 to 32; or

(iii) the PD-L1 polypeptide consists of up to 50 consecutive amino acids of SEQ ID NO: 14, and wherein said consecutive amino acids comprise the sequence of any one of SEQ ID NOs: 15, 25, 28 or 32; or

(iv) the PD-L1 polypeptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32); or

(v) the IDO1 polypeptide comprises or consists of the sequence of ALLEIASCL (SEQ ID NO: 2) or the sequence of DTLLKALLEIASCLEKALQVF (SEQ ID NO: 3) and the PD-L1 polypeptide comprises or consists of the sequence of FMTYWHLLNAFTVTVPKDL (SEQ ID NO: 32).

5. The use according to any one of claims 1-4, wherein the immune checkpoint inhibitor is an antibody or small molecule inhibitor (SMI), optionally wherein:

(i) the SMI is an inhibitor of IDO1, further optionally wherein the SMI is selected from Epacadostat (INCB24360), Indoximod, GDC-0919 (NLG919), and F001287; or

(ii) the antibody binds to CTLA4 or PD1, optionally wherein the antibody that binds to CTLA4 is ipilimumab or the antibody that binds to PD-1 is pembrolizumab or nivolumab.

6. The use according to any one of claims 1-5, wherein (a) and (b) are to be administered as a first composition and (c) is administered as a second composition, or wherein (a), (b), and (c) are to be administered as one composition.

7. The use according to claim 6, wherein the compositions further comprise an adjuvant or carrier, optionally wherein the adjuvant is selected from herein said adjuvant is a Montanide ISA adjuvant, a bacterial DNA adjuvant, an oil/surfactant adjuvant, a viral dsRNA adjuvant, an imidazoquinoline, and GM-CSF, further optionally wherein the Montanide ISA adjuvant is selected from Montanide ISA 51 and Montanide ISA 720.

8. The use according to any one of claims 1-7, wherein the use is for preventing disease progression or reducing tumor volume and wherein the disease does not progress for at least 12 months, at least 2 years, at least 3 years, at least 4 years, at least 5 years, or longer after completion of treatment.

9. The use according to any one of claims 1-8, wherein:

(i) the cancer is selected from prostate cancer, brain cancer, breast cancer, colorectal cancer, pancreatic cancer, ovarian cancer, lung cancer, cervical cancer, liver cancer, head/neck/throat cancer, skin cancer, bladder cancer, or a hematologic cancer; and/or

(ii) the cancer is a solid tumor cancer selected from an adenoma, an adenocarcinoma, a blastoma, a carcinoma, a desmoid tumour, a desmopolastic small round cell tumour, an endocrine tumour, a germ cell tumour, a lymphoma, a leukaemia, a sarcoma, a Wilms tumour, a lung tumour, a colon tumour, a lymph tumour, a breast tumour, or a melanoma, for example metastatic melanoma; and/or

(iii) the subject has an immune profile indicative of response to treatment with the first immune checkpoint polypeptide or the polynucleotide encoding the same, the second immune checkpoint polypeptide or the polynucleotide encoding the same, and the immune checkpoint inhibitor.

10. The use according to any one of claims 4-9, wherein the subject has an immune profile indicative of response to treatment with the IDO polypeptide or polynucleotide encoding the same, the PD-L1 polypeptide or polynucleotide encoding the same, and the anti-PD1 antibody, optionally wherein the immune profile comprises one or more of the following:

a) a decrease in CD4+ T regulatory cells compared to a control subject group;
b) a decrease in $CD28^{+}CD4^{+}$ T cells compared to a control subject group;
c) an increase in LAG-3+ CD4+ T cells compared to a control subject group;
d) a decrease in monocytic-myeloid derived suppressor cells (mMDSCs) compared to a control subject group;
e) an increase in $CD56^{dim}$CD16+ Natural Killer (NK) cells compared to a control subject group;
f) a decrease in $CD56^{bright}$CD16- NK cells compared to a control subject group; and/or
g) an increase in conventional dendritic cells type 2 (cDC2) compared to a control subject group,

further optionally wherein the cell populations are determined by FACS analysis of a peripheral blood sample obtained from the subject.

11. A kit comprising:

a) a first immune checkpoint polypeptide or a polynucleotide encoding the same;

b) a second immune checkpoint polypeptide or a polynucleotide encoding the same; and
c) an immune checkpoint inhibitor.

12. The kit of claim 11, wherein (a) and (b) are provided as a single composition, in a separate sealed container from (c).

13. Use of an immunotherapeutic composition in the manufacture of a medicament for the prevention or treatment of cancer in a subject, the immunotherapeutic composition comprising (a) and/or (b) as defined in claim 1, which is formulated for administration before, concurrently with, and/or after an immune checkpoint inhibitor.

14. The use according to claim 13, wherein the subject has an immune profile indicative of response to treatment with the first immune checkpoint polypeptide or the polynucleotide encoding the same, the second immune checkpoint polypeptide or the polynucleotide encoding the same, and the immune checkpoint inhibitor.

15. The use according to claim 14, wherein the first immune polypeptide is an IDO1 polypeptide, the second immune polypeptide is a PD-L1 polypeptide and the immune checkpoint inhibitor is an antibody that binds to PD1.

16. The use according to claim 14 or 15, wherein the immune profile comprises one or more of the following:

a) a decrease in CD4+ T regulatory cells compared to a control subject group;
b) a decrease in $CD28^{+}CD4^{+}$ T cells compared to a control subject group;
c) an increase in LAG-3+ CD4+ T cells compared to a control subject group;
d) a decrease in monocytic-myeloid derived suppressor cells (mMDSCs) compared to a control subject group;
e) an increase in $CD56^{dim}CD16+$ Natural Killer (NK) cells compared to a control subject group;
f) a decrease in $CD56^{bright}CD16-$ NK cells compared to a control subject group; and/or
g) an increase in conventional dendritic cells type 2 (cDC2) compared to a control subject group,

optionally wherein the cell populations are determined by FACS analysis of a peripheral blood sample obtained from the subject.

17. A method for stratifying a cancer patient into one of at least two treatment groups, wherein said method comprises analysing one or more cell populations in a peripheral blood sample from the patient to determine an immune profile; and:

i. stratifying the patient into a first treatment group if the immune profile determined is indicative of response to treatment with an IDO1 polypeptide, a PD-L1 polypeptide and an antibody that binds to PD1; or

ii. stratifying the patient into a second treatment group if the immune profile determined in step i. indicates that the subject will not respond to said treatment,

optionally wherein the first treatment group is to be treated, or is treated with, the IDO1 polypeptide, the PD-L1 polypeptide and the antibody that binds to PD1 and the second treatment group is to be treated with, or is treated with, one or more alternative therapies, and/or wherein the immune profile is a baseline immune profile.

18. The method of claim 17, wherein an immune profile indicative of response to treatment comprises or more of:

a) a decrease in $CD4^+$ T regulatory cells compared to a control subject population;

b) a decrease in $CD28^+CD4^+$ T cells compared to a control subject population;

c) an increase in LAG-3^+ $CD4^+$ T cells compared to a control subject population;

d) a decrease in monocytic-myeloid derived suppressor cells (mMDSCs), compared to a control subject population;

e) an increase in $CD56^{dim}CD16^+$ Natural Killer (NK) cells compared to a control subject population;

f) a decrease in $CD56^{bright}$CD16- Natural Killer (NK) cells compared to a control subject population; and

g) an increase in conventional dendritic cells type 2 (cDC2) compared to a control subject population.

19. A method of monitoring the response of a cancer patient to treatment with an IDO1 polypeptide, a PD-L1 polypeptide and an antibody that binds to PD1, wherein said method comprises analysing one or more cell populations in a peripheral blood sample from the patient to determine an immune profile, and:

i. determining that the patient is responding to treatment if the patient has an immune profile indicative of response to treatment; or

ii. determining that the patient is not responding to treatment if the patient does not have an immune profile indicative of response to treatment.

20. The method of claim 19, wherein the immune profile indicative of response to treatment comprises increased expression of CD28, HLA-DR, CD39, TIGIT and/or TIM-3 on CD4+ T cells and/or increased expression of HLA-DR, CD39, LAG-3 and/or TIGIT on CD8+ T-cells.

21. The method of any one of claims 17-20, wherein the IDO1 polypeptide is as defined in claim 4 and/or the PD-L1 polypeptide is as defined in claim 4 and/or the antibody that binds to PD1 is pembrolizumab or nivolumab.

22. The method of any one of claims -17-21, wherein the cancer patient has a metastatic melanoma.