

The present disclosure also provides a virus-specific immune cell or a pharmaceutical composition according to the present disclosure, for use in a method of treating or preventing a cancer.

The present disclosure also provides the use of a virus-specific immune cell or a pharmaceutical composition according to the present disclosure, in the manufacture of a medicament for treating or preventing a cancer. In one example, the present disclosure refers to use of a virus-specific immune cell comprising a chimeric antigen receptor (CAR) or nucleic acid encoding a CAR in the manufacture of a medicament for use in treating or preventing a cancer, wherein the CAR comprises: (i) an antigen-binding domain which binds specifically to CD30, (ii) a transmembrane domain, and (iii) a signalling domain, wherein the signalling domain comprises: (a) an amino acid sequence derived from the intracellular domain of CD28, and (b) an amino acid sequence comprising an immunoreceptor tyrosine-based activation motif (ITAM).

In one aspect, the present disclosure refers to use of a virus-specific immune cell comprising a chimeric antigen receptor (CAR) or nucleic acid encoding a CAR in the manufacture of a medicament for treating or preventing a cancer and reducing the risk of graft-versus-host disease (GVHD) and/or depleting alloreactive immune cells during treatment of the cancer, wherein the CAR comprises: (i) an antigen-binding domain which binds specifically to CD30, (ii) a transmembrane domain, and (iii) a signalling domain, wherein the signalling domain comprises: (a) an amino acid sequence derived from the intracellular domain of CD28, and (b) an amino acid sequence comprising an immunoreceptor tyrosine-based activation motif (ITAM).

The present disclosure also provides a method of treating or preventing a cancer comprising administering to a subject a therapeutically or prophylactically effective quantity of virus-specific immune cells or a pharmaceutical composition according to the present disclosure.

In some examples, the cancer is selected from the group consisting of: a CD30-positive cancer, an EBV-associated cancer, a hematological cancer, a myeloid hematologic malignancy, a hematopoietic malignancy, a lymphoblastic hematologic malignancy, myelodysplastic syndrome, leukemia, T cell leukemia, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, B cell non-Hodgkin's lymphoma, diffuse large B cell lymphoma, primary mediastinal B cell lymphoma, EBV-associated lymphoma, EBV-positive B cell lymphoma, EBV-positive diffuse large B cell lymphoma, EBV-positive lymphoma associated with X-linked lymphoproliferative disorder, EBV-positive lymphoma associated with HIV infection/AIDS, oral hairy leukoplakia, Burkitt's lymphoma, post-transplant lymphoproliferative disease, central nervous system lymphoma, anaplastic large cell lymphoma, T cell lymphoma, ALK-positive anaplastic T cell lymphoma, ALK-negative anaplastic T cell lymphoma, peripheral T cell lymphoma, cutaneous T cell lymphoma, NK-T cell lymphoma, extra-nodal NK-T cell lymphoma, thymoma, multiple myeloma, a solid cancer, epithelial cell cancer, gastric cancer, gastric carcinoma, gastric adenocarcinoma, gastrointestinal adenocarcinoma, liver cancer, hepatocellular carcinoma, cholangiocarcinoma, head and neck cancer, head and neck squamous cell carcinoma, oral cavity cancer, oropharyngeal cancer, oropharyngeal carcinoma, oral cancer, laryngeal cancer, nasopharyngeal carcinoma, oesophageal cancer, colorectal cancer, colorectal carcinoma, colon cancer, colon carcinoma, cervical carcinoma, prostate cancer, lung cancer, non-small cell lung cancer, small cell lung cancer, lung adenocarcinoma, squamous lung cell carcinoma, bladder cancer, urothelial carcinoma, skin cancer, melanoma, advanced melanoma, renal cell cancer, renal cell carcinoma, ovarian cancer, ovarian carcinoma, mesothelioma, breast cancer, brain cancer, glioblastoma,

prostate cancer, pancreatic cancer, mastocytosis, advanced systemic mastocytosis, germ cell tumor or testicular embryonal carcinoma.

5 The present disclosure also provides a virus-specific immune cell or a pharmaceutical composition according to the present disclosure, for use in a method of treating or preventing a disease or condition characterised by an alloreactive immune response.

Claims:

1. Use of a virus-specific immune cell comprising a chimeric antigen receptor (CAR) or nucleic acid encoding a CAR in the manufacture of a medicament for treating or preventing a cancer and reducing the risk of graft-versus-host disease (GVHD) and/or depleting alloreactive immune cells during treatment of the cancer, wherein the CAR comprises: (i) an antigen-binding domain which binds specifically to CD30, (ii) a transmembrane domain, and (iii) a signalling domain, wherein the signalling domain comprises: (a) an amino acid sequence derived from the intracellular domain of CD28, and (b) an amino acid sequence comprising an immunoreceptor tyrosine-based activation motif (ITAM).
2. The use according to claim 1, wherein the signalling domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:26.
3. The use according claim 1 or claim 2, wherein the transmembrane domain is derived from the transmembrane domain of CD28.
4. The use according to any one of claims 1 to 3, wherein the transmembrane domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:20.
5. The use according to any one of claims 1 to 4, wherein the antigen-binding domain comprises an amino acid sequence having at least 90% amino acid sequence identity to SEQ ID NO:14, and an amino acid sequence having at least 90% amino acid sequence identity to SEQ ID NO:15.
6. The use according to any one of claims 1 to 5, wherein the antigen-binding domain comprises an amino acid sequence having at least 90% amino acid sequence identity to SEQ ID NO:18.
7. The use according to any one of claims 1 to 6, wherein the signalling domain comprises: (a) an amino acid sequence derived from the intracellular domain of CD3 ζ .
8. The use according to any one of claims 1 to 7, wherein the signalling domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:25.
9. The use according to any one of claims 1 to 8, wherein the CAR additionally comprises a hinge region provided between the antigen-binding domain and the transmembrane domain.
10. The use according to claim 9, wherein the hinge region comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:33.
11. The use according to any one of claims 1 to 10, wherein the CAR comprises an amino acid sequence having at least 90% amino acid sequence identity to SEQ ID NO:35 or 36.

12. The use according to any one of claims 1 to 11, wherein the virus-specific immune cell further comprises a CAR comprising an antigen-binding domain which binds specifically to a target antigen other than CD30, or nucleic acid encoding a CAR comprising an antigen-binding domain which binds specifically to a target antigen other than CD30.

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13. The use according to any one of claims 1 to 12, wherein:

the CAR comprises: (i) an antigen-binding domain which binds specifically to CD30, (ii) a transmembrane domain, and (iii) a signalling domain comprising an immunoreceptor tyrosine-based activation motif (ITAM) and an amino acid sequence derived from the intracellular domain of CD28; and

10 wherein the virus-specific immune cell further comprises a CAR comprising an antigen-binding domain which binds specifically to a target antigen other than CD30, or nucleic acid encoding a CAR comprising an antigen-binding domain which binds specifically to a target antigen other than CD30.

14. The use according to claim 12 or claim 13, wherein the virus-specific immune cell comprises more than one non-identical CAR, or nucleic acid encoding more than one non-identical CAR.

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15. The use according to any one of claims 12 to 14, wherein the target antigen other than CD30 is a cancer cell antigen.

16. The use according to any one of claims 12 to 15, wherein the target antigen other than CD30 is selected from CD19, CD20, CD22, ROR1R, CD4, CD7, CD38, BCMA, Mesothelin, EGFR, GPC3, MUC1, HER2, GD2, CEA, EpCAM, LeY and PSCA.

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17. The use according to any one of claims 12 to 16, wherein the target antigen other than CD30 is CD19.

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18. The use according to any one of claims 1 to 17, wherein the virus-specific immune cell is a virus-specific T cell.

19. The use according to any one of claims 1 to 18, wherein the virus-specific immune cell is specific for Epstein-Barr virus (EBV).

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20. The use according to any one of claims 1 to 19, wherein the cancer is selected from the group consisting of: a CD30-positive cancer, an EBV-associated cancer, a hematological cancer, a myeloid hematologic malignancy, a hematopoietic malignancy a lymphoblastic hematologic malignancy, myelodysplastic syndrome, leukemia, T cell leukemia, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, lymphoma, non-Hodgkin's lymphoma, B cell non-Hodgkin's lymphoma, diffuse large B cell lymphoma, EBV-associated lymphoma, EBV-positive B cell lymphoma, EBV-positive diffuse large B cell lymphoma, EBV-positive lymphoma associated with X-linked lymphoproliferative disorder, EBV-positive lymphoma associated with HIV infection/AIDS, oral hairy leukoplakia, Burkitt's lymphoma, post-transplant lymphoproliferative disease, central nervous system lymphoma, anaplastic

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large cell lymphoma, T cell lymphoma, peripheral T cell lymphoma, cutaneous T cell lymphoma, NK-T cell lymphoma, extra-nodal NK-T cell lymphoma, thymoma, multiple myeloma, a solid cancer, epithelial cell cancer, gastric cancer, gastric carcinoma, gastric adenocarcinoma, gastrointestinal adenocarcinoma, liver cancer, hepatocellular carcinoma, cholangiocarcinoma, head and neck cancer, head and neck squamous cell carcinoma, oral cavity cancer, oropharyngeal cancer, oropharyngeal carcinoma, oral cancer, laryngeal cancer, nasopharyngeal carcinoma, oesophageal cancer, colorectal cancer, colorectal carcinoma, colon cancer, colon carcinoma, cervical carcinoma, prostate cancer, lung cancer, non-small cell lung cancer, small cell lung cancer, lung adenocarcinoma, squamous lung cell carcinoma, bladder cancer, urothelial carcinoma, skin cancer, melanoma, advanced melanoma, renal cell cancer, renal cell carcinoma, ovarian cancer, ovarian carcinoma, mesothelioma, breast cancer, brain cancer, glioblastoma, prostate cancer, pancreatic cancer, mastocytosis, advanced systemic mastocytosis, germ cell tumor or testicular embryonal carcinoma.