Non Patent Document 2: Daniel S. Chen and Ira Mellman, Nature, 2017, Vol. 541, p. 321-330
Non Patent Document 3: Yuqiao Shen and John Nemunaitis, Molecular Therapy, 2005, Vol. 11, No. 2, p. 180-195

SUMMARY

[0007]

An object of the present disclosure is to provide a cancer therapy by combination use of oncolytic vaccinia virus and an immune checkpoint inhibitor, and a pharmaceutical composition and a combined medicine for use in the cancer therapy.

[0008]

The present inventors surprisingly found, in developing combination use of a genetically modified vaccinia virus with another type of cancer therapy, that if vaccinia virus containing two polynucleotides, i.e., a polynucleotide encoding IL-7 and a polynucleotide encoding IL-12, are used in combination with an immune checkpoint inhibitor (for example, anti-PD-1 antibody and anti-CTLA-4 antibody), an excellent antitumor effect is exerted and excellent complete remission induction effect is provided on a remote tumor to which vaccinia virus is not administered (Example 1). Based on the finding, the present disclosure was accomplished.

[0009]

According to the present disclosure, the following disclosures are provided.

[1] A pharmaceutical composition comprising vaccinia virus as an active ingredient for use in treating cancer, wherein the vaccinia virus is

(1) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and vaccinia virus comprising a polynucleotide encoding interleukin-12 (IL-12); or

(2) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and a polynucleotide encoding interleukin-12 (IL-12) and is to be used in combination with an immune checkpoint inhibitor.

[2] The pharmaceutical composition according to [1], wherein the vaccinia virus is vaccinia virus comprising a polynucleotide encoding IL-7 and a polynucleotide encoding IL-12.

[3] The pharmaceutical composition according to [1] or [2], wherein the vaccinia virus is defective in functions of vaccinia virus growth factors (VGF) and O1L.

[4] The pharmaceutical composition according to [3], wherein the vaccinia virus lacks an SCR (short consensus repeat) domain in a B5R extracellular region.

[5] The pharmaceutical composition according to any one of [1] to [4], wherein the vaccinia virus is vaccinia virus LC16mO strain.

(1) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and vaccinia virus comprising a polynucleotide encoding interleukin-12 (IL-12); or

(2) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and a polynucleotide encoding interleukin-12 (IL-12); and

is to be used in combination with an immune checkpoint inhibitor.

[0010]

The oncolytic vaccinia virus for use in treating cancer (particularly, oncolytic vaccinia virus containing two polynucleotides, i.e., a polynucleotide encoding IL-7 and a polynucleotide encoding IL-12), if it is used in combination with an immune checkpoint inhibitor (for example, an antibody inhibiting the binding between PD-1 and PD-L1, or anti-CTLA-4 antibody), can further improve its antitumor effect.

[0010a]

In one aspect, the present disclosure refers to the use of a composition comprising vaccinia virus as an active ingredient in the manufacture of a first medicament, wherein the vaccinia virus is (1) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and vaccinia virus comprising a polynucleotide encoding interleukin-12 (IL-12); or (2) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and a polynucleotide encoding interleukin-12 (IL-12), and an immune checkpoint inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating cancer. In another aspect, the present disclosure refers to the use of a pharmaceutical composition comprising vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7); and a pharmaceutical composition comprising a vaccinia virus comprising a polynucleotide encoding interleukin-12 (IL-12) in the manufacture of a medicament for combinatorial therapy for treating cancer wherein said medicament is to be administered in combination with an immune checkpoint inhibitor. In another aspect, the present disclosure refers to the use of the pharmaceutical composition as disclosed herein or the medicament as disclosed herein; and a pharmaceutical composition comprising an immune

checkpoint inhibitor for combination therapy for treating cancer. In yet another aspect, the present disclosure refers to the use of an immune checkpoint inhibitor in the manufacture of a medicament for treating cancer, wherein said medicament is to be administered in combination with the pharmaceutical composition as disclosed herein or the medicament as disclosed herein.

BRIEF DESCRIPTION OF THE DRAWING

[0011]

FIG. 1 shows graphs exhibiting effects (tumor volume and number of mice having complete remission) of combination use of IL-12 and IL-7-carrying vaccinia virus and an anti-PD-1 antibody or an anti-CTLA-4 antibody, in tumor-bearing mice. In each graph, the vertical axis

What is claimed is:

1. Use of a composition comprising vaccinia virus as an active ingredient in the manufacture of a first medicament, wherein the vaccinia virus is

(1) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and vaccinia virus comprising a polynucleotide encoding interleukin-12 (IL-12); or

(2) vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7) and a polynucleotide encoding interleukin-12 (IL-12), and an immune checkpoint inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating cancer.

2. The use according to Claim 1, wherein the vaccinia virus is vaccinia virus comprising a polynucleotide encoding IL-7 and a polynucleotide encoding IL-12.

3. The use according to Claim 1 or 2, wherein the vaccinia virus is defective in functions of vaccinia virus growth factors (VGF) and O1L.

4. The use according to Claim 3, wherein the vaccinia virus lacks an SCR (short consensus repeat) domain in a B5R extracellular region.

5. The use according to any one of Claims 1 to 4, wherein the vaccinia virus is vaccinia virus LC16mO strain.

6. The use according to any one of Claims 1 to 5, wherein the immune checkpoint inhibitor is an antibody selected from the group consisting of an anti-PD-1 antibody, an anti-PD-L1 antibody and an anti-CTLA-4 antibody, or an antigen-binding fragment thereof.

7. The use according to any one of Claims 1 to 6, wherein the cancer is solid cancer.

8. The use according to any one of Claims 1 to 7, wherein the cancer is metastatic cancer.

9. Use of a pharmaceutical composition comprising vaccinia virus comprising a polynucleotide encoding interleukin-7 (IL-7); and a pharmaceutical composition comprising a vaccinia virus comprising a polynucleotide encoding interleukin-12 (IL-12) in the manufacture of a medicament for combinatorial therapy for treating cancer wherein said medicament is to be administered in combination with an immune checkpoint inhibitor.

10. Use of the pharmaceutical composition as defined in any one of Claims 1 to 8 or the medicament as defined in

Claim 9; and a pharmaceutical composition comprising an immune checkpoint inhibitor for combination therapy for treating cancer.

11. Use of an immune checkpoint inhibitor in the manufacture of a medicament for treating cancer, wherein said medicament is to be administered in combination with the pharmaceutical composition as defined in any one of Claims 1 to 8 or the medicament as defined in Claim 9.