METHODS FOR TREATING CANCER

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application no. 62/846,064, filed May 10, 2019, the content of which is incorporated by reference herein in its entirety.

TECHNICAL FIELD OF THE INVENTION

[0002] The present invention relates to use of a Bicycle toxin conjugate BT1718, or a pharmaceutically acceptable salt thereof, in combination with a checkpoint inhibitor, for treating cancer. The present invention also provides pharmaceutically acceptable compositions comprising BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor.

BACKGROUND OF THE INVENTION

[0003] MT1-MMP is a transmembrane metalloprotease that plays a major role in the extracellular matrix remodelling, directly by degrading several of its components and indirectly by activating pro-MMP2. MT1-MMP is crucial for tumor angiogenesis (Sounni *et al* (2002) FASEB J. 16(6), 555-564) and is over-expressed on a variety of solid tumors. Accordingly, there remains a high unmet need in developing inhibitors of MT1-MMP for the treatment of cancer.

SUMMARY

[0003a] In an aspect of the present disclosure, there is provided a use of BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor, in the manufacture of a medicament for treating a cancer in a patient.

[0003b] In another aspect of the present disclosure, there is provided a use of BT1718, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein the medicament is used in combination with a checkpoint inhibitor.

[0004] It has now been found that a combination of BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor vastly improves anti-tumor activity compared to each of the single agent treatment. Accordingly, in one example, the present disclosure provides a

composition comprising BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor.

[0005] In another example, the present disclosure provides a method for treating a cancer in a patient, comprising administering to the patient a therapeutically effective amount of BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor.

CLAIMS

We claim:

1. Use of BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor, in the manufacture of a medicament for treating a cancer in a patient.

2. The use of claim 1, wherein the cancer is a lung cancer.

3. The use of claim 2, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a dose of 9 mg/m^2.

4. The use of claim 2, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a dose of 30 mg/m^2.

5. The use of any one of claims 2-4, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a frequency of 2 times a week.

6. The use of claim 2, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a dose of 14.4 mg/m^2.

7. The use of claim 6, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a frequency of once a week.

8. The use of any one of claims 2-7, wherein the checkpoint inhibitor is an anti-PD1 antibody.

9. The use of claim 1, wherein the cancer is a breast cancer.

10. The use of claim 9, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a dose of 14.4 mg/m^2.

11. The use of claim 9, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a dose of 18.6 mg/m^2.

12. The use of any one of claims 9-11, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a frequency of once a week.

13. The use of any one of claims 9-12, wherein the checkpoint inhibitor is an anti-PD1 antibody.

14. The use of claim 1, wherein the cancer is a colon cancer.

15. The use of claim 14, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a dose of 19.2 mg/m^2.

16. The use of claim 14 or 15, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a frequency of once a week.

17. The use of any one of claims 14-16, wherein the checkpoint inhibitor is an anti-CTLA4 antibody.

18. The use of any one of the preceding claims, wherein BT1718, or a pharmaceutically acceptable salt thereof, and the checkpoint inhibitor are to be administered by an intravenous infusion.

19. Use of BT1718, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein the medicament is used in combination with a checkpoint inhibitor.

20. The use of claim 19, wherein the medicament further comprises histidine.

21. The use of claim 19, wherein the medicament further comprises sucrose.

22. The use of claim 19, wherein the medicament is a formulation comprising BT1718, or a pharmaceutically acceptable salt thereof, histidine, sucrose, and water, at about pH 7.