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 a combination therapy for treating a cancer in a patient, wherein the checkpoint inhibitor is an antibody and the cancer is breast cancer or colon cancer.

[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 to be used in combination with a checkpoint inhibitor, wherein the checkpoint inhibitor is an antibody and the cancer is breast cancer or colon cancer.

[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

CLAIMS

We claim:

1. Use of BT1718, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor, in the manufacture of a medicament for a combination therapy for treating a cancer in a patient, wherein the checkpoint inhibitor is an antibody and the cancer is breast cancer or colon cancer.

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

~~10~~3. The use of claim ~~9~~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.

~~11~~4. The use of claim ~~9~~2, 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~~5. The use of any one of claims ~~9-11~~2-4, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a frequency of once a week.

~~13~~6. The use of any one of claims ~~9-12~~2-5, wherein the checkpoint inhibitor is an anti-PD1 antibody.

~~14~~7. The use of claim 1, wherein the cancer is a colon cancer.

~~15~~8. The use of claim ~~14~~7, 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~~9. The use of claim ~~14-~~7 or ~~15~~8, wherein BT1718, or a pharmaceutically acceptable salt thereof, is to be administered to the patient at a frequency of once a week.

~~17~~10. The use of any one of claims ~~14-16~~7-9, wherein the checkpoint inhibitor is an anti-CTLA4 antibody.

~~18~~11. 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~~12. Use of BT1718, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein the medicament is to be used in combination with a checkpoint inhibitor, wherein the checkpoint inhibitor is an antibody and the cancer is breast cancer or colon cancer.

~~20~~13. The use of claim ~~19~~12, wherein the medicament further comprises histidine.

~~21~~14. The use of claim ~~19~~12, wherein the medicament further comprises sucrose.

~~22~~15. The use of claim ~~19~~12, wherein the medicament is a formulation comprising BT1718, or a pharmaceutically acceptable salt thereof, histidine, sucrose, and water, at about pH 7.