Thus, the instant disclosure relates to combinations of iadademstat, or a pharmaceutically acceptable salt or solvate thereof, with PD(L)1 inhibitors (as defined herein).

Accordingly, in one ~~aspect~~example, the present disclosure provides a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor. In one aspect, the present disclosure provides a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor. In another aspect, the present disclosure provides a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for use in therapy, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor. In yet another aspect, the present disclosure provides a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for use in the treatment of a disease, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.

The present disclosure further provides a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for use in the treatment of cancer.

The present disclosure further provides a method for treating cancer in a patient (preferably a human) in need thereof, comprising administering to the patient a therapeutically effective amount of a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor.

The present disclosure further provides a method for treating cancer in a patient (preferably a human) in need thereof, comprising administering to the patient a therapeutically effective amount of iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a therapeutically effective amount of a PD(L)1 inhibitor.

In one ~~aspect~~example, the present disclosure further provides the use of iadademstat, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for the treatment of cancer to be used in combination with a PD(L)1 inhibitor. In one aspect, the present disclosure provides use of iadademstat, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for the treatment of cancer to be used in combination with a PD(L)1 inhibitor, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor. In another aspect, the present disclosure provides use of a PD(L)1 inhibitor for the manufacture of a medicament for the treatment of cancer to be used in combination with iadademstat or a pharmaceutically acceptable salt or solvate thereof, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor. In yet another aspect, the present disclosure provides use of a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for the manufacture of a medicament for the treatment of cancer, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.

The present disclosure further provides the use of a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for the treatment of cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the effect of treatment with a combination of iadademstat (referred to as "ORY-1001") and a PD(L)1 inhibitor (triangles) in comparison with treatment with the PD(L)1 inhibitor alone (squares) on tumor volume in the mice B16F10 melanoma model, as explained in more detail in Example 1. Data is represented as mean± standard error of the mean (SEM); p=0.004.

Figure 2 shows the effect of treatment with a combination of iadademstat ("ORY-1001") and a PD(L)1 inhibitor (triangles) in comparison with treatment with the PD(L)1 inhibitor alone (squares) on tumor weight in the same mice B16F10 melanoma model, as explained in more detail in Example 1. Data is represented as mean± standard error of the mean (SEM); p=0.001.

DETAILED DESCRIPTION OF THE INVENTION

As indicated above, the present invention is based on the discovery that the combination of iadademstat with PD(L)1 inhibitors exhibits outstanding anticancer activity, with superior anticancer efficacy as compared to treatment with the PD(L)1 inhibitor alone. The combined treatment with iadademstat and a PD(L)1 inhibitor causes a significant increase in the antitumor effect as compared to treatment with the PD(L)1 inhibitor alone, as illustrated in Example 1 and in Figures 1 and 2 using an *in vivo* murine melanoma model. Treatment with the combination produces statistically significant reductions in both the tumor volume and tumor weight compared

CLAIMS

1. A combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.
2. A combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for use in therapy, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.
3. A combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for use in the treatment of a disease, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.
4. Use of iadademstat, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for the treatment of cancer to be used in combination with a PD(L)1 inhibitor, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.
5. Use of a PD(L)1 inhibitor for the manufacture of a medicament for the treatment of cancer to be used in combination with iadademstat or a pharmaceutically acceptable salt or solvate thereof, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.
6. Use of a combination comprising iadademstat, or a pharmaceutically acceptable salt or solvate thereof, and a PD(L)1 inhibitor for the manufacture of a medicament for the treatment of cancer, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.

~~7. The combination according to claim 1, the combination for use according to claim 2 or 3, or the use according to any one of claims 4 to 6, wherein the PD(L)1 inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor.~~

~~8.~~7. The combination according to claim 1 ~~or 7~~, the combination for use according to ~~any one of~~ claim~~s~~ 2~~,~~ or 3 ~~or 7~~, or the use according to any one of claims 4 to ~~7~~6, wherein the PD(L)1 inhibitor is selected from the group consisting of Pembrolizumab, Nivolumab, Cemiplimab, Camrelizumab, Tislelizumab, Sintilimab, Toripalimab, Spartalizumab, AGEN-2034, AK-103, AK-104, AK-105, AK-112, AK-123, AM-0001, AMP-224, AT16201, BCD-100, BH-2950, BH-2996h, BI-754091, BMS-1001, BMS-1166, CS-1003, CX-188, ENUM-244C8, GLS-010, hAb21, HLX-10, IKT-202, JNJ-63723283, JTX-4014, KN0-46, MEDI-0680, MGA-012, MGD-013, PF-06801591, PRS-332, RO7121661, STI-A1110, TSR-042, XmAb-20717, Atezolizumab, Avelumab, Durvalumab, AK-106, APL-502, AVA-004, BGB-A333, BH-2996h, BMS-936559, CA-170, CA-327, CBA-0710, CK-301, CS-1001, CX-072, FAZ-053, FS-118, GR1405, HLX-20, IKT-201, JS-003, KD033, KN-035, KY-1003, LY3300054, M-7824, MCLA-145, MSB-2311, and SHR-1316.

~~9.~~8. The combination according to ~~any one of~~ claim~~s~~ 1~~, 7~~ or ~~8~~7, the combination for use according to any one of claims 2, 3~~, 7~~ or ~~8~~7, or the use according to any of claims 4 to ~~8~~7, wherein the PD(L)1 inhibitor is selected from the group consisting of Pembrolizumab, Nivolumab, Cemiplimab, Atezolizumab, Avelumab and Durvalumab.

10.9. The combination according to claim 1 ~~or 7~~, the combination for use according to ~~any one of~~ claim~~s~~ 2~~, 3~~ or ~~7~~3, or the use according to any one of claims 4 to ~~7~~6, wherein the PD(L)1 inhibitor is a PD-1 inhibitor.

11.10. The combination according to claim ~~10~~9, the combination for use according to claim ~~10~~9, or the use according to claim ~~10~~9, wherein the PD-1 inhibitor is selected from the group consisting of Pembrolizumab, Nivolumab, Cemiplimab, Camrelizumab, Tislelizumab, Sintilimab, Toripalimab, Spartalizumab, AGEN-2034, AK-103, AK-104, AK-105, AK-112, AK-123, AM-0001, AMP-224, AT16201, BCD-100, BH-2950, BH-2996h, BI-754091, BMS-1001, BMS-1166, CS-1003, CX-188, ENUM-244C8, GLS-010, hAb21, HLX-10, IKT-202, JNJ-63723283, JTX-4014, KN0-46, MEDI-0680, MGA-012, MGD-013, PF-06801591, PRS-332, RO7121661, STI-A1110, TSR-042, and XmAb-20717.

12.11. The combination according to claim ~~10~~ 9 or ~~11~~10, the combination for use according to claim ~~10~~ 9 or ~~11~~10, or the use according to claim ~~10~~ 9 or ~~11~~10, wherein the PD-1 inhibitor is selected from the group consisting of Pembrolizumab, Nivolumab and Cemiplimab.

13.12. The combination according to claim 1 ~~or 7~~, the combination for use according to ~~any one of~~ claim~~s~~ 2~~, 3~~ or ~~7~~3, or the use according to any one of claims 4 to ~~7~~6, wherein the PD(L)1 inhibitor is a PD-L1 inhibitor.

14.13. The combination according to claim ~~13~~12, the combination for use according to claim ~~13~~12, or the use according to claim ~~13~~12, wherein the PD-L1 inhibitor is selected from the group consisting of Atezolizumab, Avelumab, Durvalumab, AK-106, APL-502, AVA-004, BGB-A333, BH-2996h, BMS-936559, CA-170, CA-327, CBA-0710, CK-301, CS-1001, CX-072, FAZ-053, FS-118, GR1405, HLX-20, IKT-201, JS-003, KD033, KN-035, KY-1003, LY3300054, M-7824, MCLA-145, MSB-2311, and SHR-1316.

15.14. The combination according to claim ~~13~~ 12 or ~~14~~13, the combination for use according to claim ~~13~~ 12 or ~~14~~13, or the use according to claim ~~13~~ 12 or ~~14~~13, wherein the PD-L1 inhibitor is selected from the group consisting of Atezolizumab, Avelumab and Durvalumab.

~~16. The combination according to claim 1, the combination for use according to claim 2 or 3, or the use according to any one of claims 4 to 6, wherein the PD(L)1 inhibitor is a PD-L2 inhibitor.~~

17.15. The use according to any one of claims 4 to ~~16~~14, wherein the cancer is selected from the group consisting of melanoma, small cell lung cancer, non-small cell lung cancer (NSCLC), head and neck cancer, renal cell carcinoma, Hodgkin lymphoma, urothelial carcinoma, colorectal cancer, hepatocellular cancer, cutaneous squamous cell carcinoma, ovarian cancer, gastric cancer, gastroesophageal cancer, Merkel cell carcinoma, nasopharyngeal cancer, breast cancer, and esophageal squamous cell carcinoma.

18.16. The use according to claim ~~17~~15, wherein the cancer is melanoma.

19.17. The use according to claim ~~17~~15, wherein the cancer is small cell lung cancer.

~~20.~~18. The use according to any one of claims 4 to ~~19~~17, wherein the cancer is a cancer that is refractory, non-responsive or relapsed to PD(L)1 inhibitor therapy.

~~21.~~19. The combination according to any one of claims 1 or 7 to ~~16~~14, the combination for use according to any one of claims 2, 3 or 7 to ~~16~~14, or the use according to any one of claims 4 to ~~20~~18, wherein iadademstat or a pharmaceutically acceptable salt or solvate thereof is iadademstat di-hydrochloride.

~~22.~~20. The combination for use according to any one of claims 2, 3, 7 to ~~16~~ 14 or ~~21~~19, or the use according to any one of claims 4 to ~~21~~19, wherein iadademstat or the pharmaceutically acceptable salt or solvate thereof is administered orally.

~~23.~~21. The combination for use according to any one of claims 2, 3, 7 to ~~16~~14, ~~21~~ 19 or ~~22~~20, or the use according to any one of claims 4 to ~~22~~20, wherein iadademstat or the pharmaceutically acceptable salt or solvate thereof and the PD(L)1 inhibitor are administered using separate formulations.

~~24.~~22. The combination for use according to any one of claims 2, 3, 7 to ~~16~~ 14 or ~~21~~ 19 to ~~23~~21, or the use according to any one of claims 4 to ~~23~~21, wherein iadademstat or the pharmaceutically acceptable salt or solvate thereof and the PD(L)1 inhibitor are administered as a simultaneous regimen.

~~25.~~23. The combination for use according to any one of claims 2, 3, 7 to ~~16~~ 14 or ~~21~~ 19 to ~~23~~21, or the use according to any one of claims 4 to ~~23~~21, wherein iadademstat or the pharmaceutically acceptable salt or solvate thereof and the PD(L)1 inhibitor are administered as a sequential regimen.