

Claims (15.06.2018):

1. An antibody or an antigen binding portion thereof that binds specifically to a human PD-1 ("an anti-PD-1 antibody") for use in treating a melanoma tumor in a human patient having a PD-L1-negative melanoma tumor in combination with an antibody or an antigen-binding portion thereof that binds specifically to a human CTLA-4 ("an anti-CTLA-4 antibody"), comprising:
 - (i) identifying the patient having a PD-L1-negative melanoma tumor; and
 - (ii) administering to the patient:
 - (a) a flat dose of 80 mg of the anti-PD-1 antibody; and
 - (b) the anti-CTLA-4 antibody.
2. An anti-PD-1 antibody for use in treating a melanoma tumor in a human patient having a PD-L1-negative melanoma tumor in combination with an anti-CTLA-4 antibody, comprising administering to the patient:
 - (a) a flat dose of 80 mg of the anti-PD-1 antibody; and
 - (b) the anti-CTLA-4 antibody.
3. The anti-PD-1 antibody for the use of claim 1, wherein the identifying comprises measuring a PD-L1 expression on the melanoma tumor.
4. The anti-PD-1 antibody for the use of claim 3, wherein the measuring comprises providing a test tissue sample obtained from the patient, the test tissue sample comprising tumor cells and/or tumor-infiltrating inflammatory cells.
5. The anti-PD-1 antibody for the use of claim 4, wherein the measuring further comprises assessing the proportion of cells in the test tissue sample that express PD-L1 on the cell surface.
6. The anti-PD-1 antibody for the use of claim 5, wherein the test tissue sample is a formalin-fixed paraffin- embedded (FFPE) tissue sample.
7. The anti-PD-1 antibody for the use of claim 6, wherein the presence of PD-L1 is determined using an automated IHC assay.

8. The anti-PD-1 antibody for the use of claim 7, wherein the IHC assay is performed using an anti-PD-L1 monoclonal antibody that specifically binds to the PD-L1 and wherein the anti-PD-L1 monoclonal antibody is selected from the group consisting of 28-8, 28-1, 28-12, 29-8, 5H1, and any combination thereof.
9. The anti-PD-1 antibody for the use of any one of claims 1 to 8, wherein the PD-L1-negative melanoma tumor is characterized by having less than about 5% of tumor cells showing binding to the anti-PD-L1 antibody or an antigen-binding portion thereof.
10. The anti-PD-1 antibody for the use of any one of claims 1 to 9, wherein the anti-PD-1 antibody is nivolumab or pembrolizumab.
11. The anti-PD-1 antibody for the use of any one of claims 1 to 10, wherein the anti-PD-1 antibody is administered once every 3 weeks..
12. The anti-PD-1 antibody for the use of any one of claims 1 to 11, wherein the anti-CTLA-4 antibody is ipilimumab.
13. The anti-PD-1 antibody for the use of any one of claims 1 to 12, wherein the anti-CTLA-4 antibody is administered at a dose of 3 mg/kg body weight once every 3 weeks.
14. The anti-PD-1 antibody for the use of any one of claims 1 to 13, wherein the anti-PD-1 antibody and the anti-CTLA-4 antibody are in a single pharmaceutical composition.
15. The anti-PD-1 antibody for the use of any one of claims 1 to 14, further comprising administering an anti-cancer agent.