

CLAIMS

1. Use of an antibody that neutralizes the inhibitory activity of human NKG2A in the preparation of a medicament for the treatment of a cancer in a human patient, in which the treatment comprises administering to the patient an effective amount of each of: (a) an
5 antibody that neutralizes the inhibitory activity of human NKG2A, and (b) an antibody that neutralizes the inhibitory activity of human PD-1.
2. Use according to Claim 1, in which at least two doses of the antibody that neutralizes the inhibitory activity of human NKG2A are to be administered in an amount effective to achieve a continuous blood concentration of anti-NKG2A antibody of at least 10 µg/ml for at
10 least one week following administration thereof.
3. Use according to Claim 1 or 2, in which the treatment comprises at least one administration cycle, optionally in which the cycle is a period of eight weeks, in which for each cycle, two, three or four doses of the antibody that neutralizes the inhibitory activity of human NKG2A are to be administered and two, three or four doses of the antibody that
15 neutralizes the inhibitory activity of PD-1 antibody are to be administered.
4. Use according to Claim 1, 2 or 3, in which the antibody that neutralizes the inhibitory activity of human NKG2A and the antibody that neutralizes the inhibitory activity of PD-1 are formulated for separate administration and are to be administered concurrently or sequentially.
5. Use according to any preceding claim, in which the antibody that neutralizes the
20 inhibitory activity of human NKG2A and the antibody that neutralizes the inhibitory activity of PD-1 are to be simultaneously administered in a single formulation.
6. Use according to any preceding claim, in which the antibody that neutralizes the inhibitory activity of human NKG2A and the antibody that neutralizes the inhibitory activity of PD-1 are to be simultaneously administered on the same day.
- 25 7. Use according to any preceding claim, in which the cancer is a solid tumor.
8. Use according to Claim 7, in which the cancer is hematological tumor.
9. Use according to Claim 7, in which the cancer is selected from the group consisting of lung cancer, renal cell carcinoma (RCC), melanoma, colorectal cancer, and ovarian cancer.

10. Use according to any of Claims 7, 8 or 9, in which the cancer is an HLA-E-expressing cancer.
11. Use according to any preceding claim, in which an antibody that neutralizes the inhibitory activity of NKG2A comprises the CDR1, CDR2 and CDR3 domains of a heavy
5 chain having the sequence set forth in any one of SEQ ID NOS: 4-8, and the CDR1, CDR2 and CDR3 domains of a light chain having the sequence set forth in SEQ ID NO: 9.
12. Use according to any preceding claim, in which an antibody that neutralizes the inhibitory activity of PD-1 is an antibody that binds a PD-1 polypeptide.
13. Use according to any preceding claim, in which an antibody that neutralizes the
10 inhibitory activity of PD-1 is an antibody that binds a PD-L1 polypeptide.
14. Use according to any preceding claim, in which the antibody is a chimeric, human or humanized antibody.
15. Use according to any preceding claim, in which the antibody that neutralizes the inhibitory activity of NKG2A is a non-depleting antibody.
- 15 16. Use according to any preceding claim, in which the antibody that neutralizes the inhibitory activity of PD-1 is a non-depleting antibody.
17. Use according to any preceding claim, in which the antibody is IgG4 antibody.
18. Use according to any preceding claim, in which the antibody lacks an Fc domain or comprises an Fc domain that is modified to reduce binding between the Fc domain and an Fcγ
20 receptor.
19. Use according to any preceding claim, in which the antibody is an antibody fragment.
20. Use according to Claim 19, in which the antibody fragment is selected from Fab, Fab', Fab'-SH, F(ab')₂, Fv, a diabody, a single-chain antibody fragment, or a multispecific antibody comprising multiple different antibody fragments.
- 25 21. A pharmaceutical composition comprising an antibody that neutralizes the inhibitory activity of NKG2A, an antibody that neutralizes the inhibitory activity of PD-1 and a pharmaceutically acceptable carrier.

22. A kit comprising: (a) a dose of an antibody that neutralizes the inhibitory activity of NKG2A and (b) a dose of an antibody that neutralizes the inhibitory activity of PD-1.
23. A kit comprising: (a) multiple packages of single-dose pharmaceutical compositions containing an effective amount of an antibody that neutralizes the inhibitory activity of NKG2A, and (b) multiple packages of single-dose pharmaceutical compositions containing an effective amount of an antibody that neutralizes the inhibitory activity of PD-1.
24. An *in vitro* method for modulating the activity of NKG2A+ PD-1+ lymphocytes, optionally CD8+ T cells, comprising bringing lymphocytes expressing at their surface NKG2A and PD-1 into contact with an antibody that neutralizes the inhibitory activity of NKG2A and an antibody that neutralizes the inhibitory activity of PD-1.
25. Use of an antibody that neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for the treatment or prevention of a cancer in an individual, in which the treatment comprises:
 - (a) determining the HLA-E polypeptide status of malignant cells within the individual having a cancer, and
 - (b) upon a determination that HLA-E polypeptides are prominently expressed by malignant cells, administering to the individual an antibody that neutralizes the inhibitory activity of a human NKG2A polypeptide and an antibody that inhibits a human PD-1 polypeptide.
26. Use of an antibody that neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for treatment or prevention of a cancer in an individual, in which the treatment comprises:
 - (a) determining the NKG2A and PD-1 polypeptide status of tumor infiltrating lymphocytes from the individual, and
 - (b) upon a determination that NKG2A and PD-1 polypeptides are expressed on the surface of a significant proportion of tumor infiltrating lymphocytes from the individual, administering to the individual a therapeutic regimen that comprises (i) an antibody that neutralizes the inhibitory activity of a human NKG2A polypeptide and (ii) an antibody that inhibits a human PD-1 polypeptide.