

CLAIMS

1. Use of an antibody that binds and neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for the treatment of cancer in an individual having a solid tumour, in which the treatment comprises administering to the individual the antibody for at least one administration cycle in which the anti-NKG2A antibody is to be administered at least twice and in amounts effective to maintain between two successive administrations of the anti-NKG2A antibody, and for a period of at least 2 weeks or one month following administration of the antibody, a blood concentration of anti-NKG2A antibody of at least 40 µg/ml, in which the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 3 and a VL comprising the amino acid sequence of SEQ ID NO: 7.
2. Use according to Claim 1, in which the anti-NKG2A antibody is to be administered at least twice and in amounts effective to maintain a continuous blood concentration of the anti-NKG2A antibody of at least 50 µg/ml throughout the administration cycle.
3. Use according to Claim 1 or 2, in which the antibody is to be administered to achieve a peak blood concentration of anti-NKG2A antibody of at least 100 µg/ml upon administration.
4. Use according to Claim 1, 2 or 3, in which the antibody is to be administered in an amount effective to provide a continuous (minimal) blood concentration of the anti-NKG2A antibody of at least 100 µg/ml for at least one week, optionally two weeks, following administration of the anti-NKG2A antibody.
5. Use according to any preceding claim, in which the antibody is to be administered to maintain a continuous (minimal) blood concentration of the anti-NKG2A antibody of at least about 100 µg/ml between two successive administrations of the anti-NKG2A antibody.
6. Use according to any preceding claim, in which the antibody is to be administered to maintain a continuous blood concentration of the anti-NKG2A antibody of at least 100 µg/ml, optionally between 100-200 µg/ml, between two successive administrations of the anti-NKG2A antibody, optionally throughout the administration cycle.
7. Use according to any preceding claim, in which the antibody is to be administered 2 times per month.

8. Use according to any preceding claim, in which the antibody is to be administered intravenously two times per month and the amount of anti-NKG2A antibody of at least 10 µg/ml between at least two successive administrations of the anti-NKG2A antibody to be administered is between 2-10 mg/kg, optionally 2-6 mg/kg, optionally 2-8 mg/kg, or optionally 2-4 mg/kg body weight.
9. Use according to any preceding claim, in which the antibody is to be administered intravenously two times per month and the amount of anti-NKG2A antibody of at least 100 µg/ml between at least two successive administrations of the anti-NKG2A antibody to be administered is between 4-10 mg/kg, optionally 4-6 mg/kg, optionally 4-8 mg/kg, optionally about 4 mg/kg, optionally about 6 mg/kg, optionally about 8 mg/kg, or optionally about 10 mg/kg body weight.
10. Use according to any preceding claim, in which the treatment comprises a loading period in which the antibody is to be administered at least once at an initial dose effective to maintain a blood concentration of at least 100 µg/ml until the next successive administration of the anti-NKG2A antibody, followed by a maintenance period in which the antibody is administered at least twice in a second dose and at a frequency effective to maintain a continuous blood concentration of the anti-NKG2A antibody of at least 100 µg/ml between successive administrations of the anti-NKG2A antibody.
11. Use according to Claim 10, in which the antibody is to be administered intravenously, and in which the loading period comprises administering the antibody once at a dose of between 8-10 mg/kg, optionally about 10 mg/kg, and the maintenance period comprises administering the antibody at least twice, at an interval of about two weeks at dose of between 2-6 mg/kg, optionally between 2-5 mg/kg, optionally between 2-4 mg/kg, optionally about 2 mg/kg, optionally about 3 mg/kg, optionally about 4 mg/kg, or optionally about 6 mg/kg body weight.
12. Use according to any preceding claim, in which the administration cycle is 8 weeks or at least 8 weeks.
13. Use according to any preceding claim, in which the administration cycle comprises at least 4 administrations of the anti-NKG2A antibody.
14. Use according to any preceding claim, in which the individual has a HNSCC.

15. Use according to any preceding claim, in which the individual has a solid tumor and is treated with the anti-NKG2A antibody prior to surgery to remove the tumor.
16. Use according to Claim 15, in which the individual is treated with a complete administration cycle of the anti-NKG2A antibody prior to surgery to remove the tumor.
- 5 17. Use according to any preceding claim, in which antibody has an EC_{50} for binding to NKG2A-expressing cells in PBMC of between 1-10 ng/ml.
18. Use according to any preceding claim, in which antibody has K_D of between 10^{-10} M and 10^{-12} M for binding to a recombinant soluble NKG2A polypeptide.
19. Use according to any preceding claim, in which the antibody comprises a human IgG4
10 constant region.
20. Use according to any preceding claim, in which the antibody comprises an Fc-engineered constant region comprising an amino acid modification that reduces binding to a human Fc γ receptor.
21. Use according to any preceding claim, in which the antibody is an antibody fragment.
- 15 22. Use according to Claim 21, in which the antibody fragment lacks an Fc domain.
23. Use according to Claim 21 or 22, in which the antibody fragment is from the group consisting of a Fab fragment, a Fab' fragment, a Fab'-SH fragment, a F(ab)² fragment, a F(ab')² fragment, an Fv fragment, a heavy chain Ig (a llama or camel Ig), a V_{HH} fragment, a single domain FV, and a single-chain antibody fragment.
- 20 24. Use according to any preceding claim, in which the anti-NKG2A antibody is administered as a pharmaceutically acceptable composition comprising a therapeutically effective amount of the anti-NKG2A antibody.
- 25 25. Use of an antibody that binds and neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for the treatment or prevention of a cancer in an individual, in
25 which the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 3 and a VL comprising the amino acid sequence of SEQ ID NO: 7, and in which the treatment comprises:

(a) determining the expression of HLA-E polypeptide on the surface of malignant cells within the individual having a cancer, and

(b) upon a determination that the patient has HLA-E polypeptides are expressed on the surface of malignant cells, administering to the individual the antibody in an amount effective to achieve a blood (serum) concentration of anti-NKG2A antibody that corresponds to at least the EC_{50} , optionally the EC_{100} , for NKG2A+ NK cell response, in which NKG2A+ NK cell response is the NKG2A+ NK cell response to an HLA-E expressing target cell.

26. Use according to Claim 25, in which determining the HLA-E polypeptide status in step

(a) comprises determining the level of expression of a HLA-E nucleic acid or polypeptide of malignant cells in a biological sample and comparing the level to a reference level.

27. Use according to Claim 25 or 26, in which the antibody is to be administered in an amount effective to achieve an extravascular tissue concentration of anti-NKG2A antibody that corresponds to at least the EC_{50} , optionally the EC_{100} , for NKG2A+ NK cell response.

28. Use according to Claim 25, 26 or 27, in which the EC_{50} for NKG2A+ NK cell response is about 4 $\mu\text{g/ml}$.

29. Use according to any of Claims 25, 26 or 27, in which the EC_{100} for NKG2A+ NK cell response is about 10 $\mu\text{g/ml}$.

30. Use according to any of Claims 25 to 29, in which antibody competes with HLA-E for binding to NKG2A.

31. Use of an antibody that binds and neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for the treatment of disease in an individual, in which the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 3 and a VL comprising the amino acid sequence of SEQ ID NO: 7, and in which the treatment comprises administering to the individual the antibody in an amount effective to achieve a blood concentration that corresponds to at least the EC_{50} , optionally the EC_{100} , for NKG2A+ NK cell response.

32. Use according to Claim 31, in which the EC_{50} for NKG2A+ NK cell response is about 4 $\mu\text{g/ml}$.

33. Use according to Claim 31, in which the EC₁₀₀ for NKG2A+ NK cell response is about 10 µg/ml.
34. Use according to any preceding claim, in which NKG2A+ NK cell response is the NKG2A+ NK cell response to an HLA-E expressing target cell.