

CLAIMS

1. Use of an anti-NKG2A 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 anti-NKG2A antibody is to be administered to the
5 individual 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 initial administration of the anti-NKG2A antibody, a blood concentration of anti-NKG2A antibody of at least 40 µg/ml, in which the anti-NKG2A antibody comprises a
10 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.
- 15 3. Use according to Claim 1 or 2, in which the anti-NKG2A 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 anti-NKG2A antibody is to be administered in an amount effective to provide a continuous (minimal) blood concentration of
20 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 anti-NKG2A 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-
25 NKG2A antibody.
6. Use according to any preceding claim, in which the anti-NKG2A 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 anti-NKG2A antibody is to be administered 2 times per month.
8. Use according to any preceding claim, in which the anti-NKG2A antibody is to be administered intravenously two times per month and the amount of anti-NKG2A antibody of
5 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 anti-NKG2A antibody is to be administered intravenously two times per month and the amount of anti-NKG2A antibody of
10 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
15 period in which the anti-NKG2A 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 anti-NKG2A antibody is to be 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
20 100 µg/ml between successive administrations of the anti-NKG2A antibody.
11. Use according to Claim 10, in which the anti-NKG2A antibody is to be administered intravenously, and in which the loading period comprises the anti-NKG2A antibody being administered once at a dose of between 8-10 mg/kg, optionally about 10 mg/kg, and the maintenance period comprises the anti-NKG2A antibody being administered at least twice, at
25 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 to be treated with the anti-NKG2A antibody prior to surgery to remove the tumor.
16. Use according to Claim 15, in which the individual is to be treated with a complete administration cycle of the anti-NKG2A antibody prior to surgery to remove the tumor.
17. Use according to any preceding claim, in which the anti-NKG2A 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 the anti-NKG2A 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 anti-NKG2A antibody comprises a human IgG4 constant region.
20. Use according to any preceding claim, in which the anti-NKG2A antibody comprises an Fc-engineered constant region comprising an amino acid modification that reduces binding to a human $Fc\gamma$ receptor.
21. Use according to any preceding claim, in which the anti-NKG2A antibody is an anti-NKG2A antibody fragment.
22. Use according to Claim 21, in which the anti-NKG2A antibody fragment lacks an Fc domain.
23. Use according to Claim 21 or 22, in which the anti-NKG2A 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.
24. Use according to any preceding claim, in which the anti-NKG2A antibody is to be administered as a pharmaceutically acceptable composition comprising a therapeutically effective amount of the anti-NKG2A antibody.

25. Use of an anti-NKG2A 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 which the anti-NKG2A 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,
5 comprising:

(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, the anti-NKG2A antibody to be administered to the
10 individual in an amount effective to achieve a blood (serum) concentration of anti-NKG2A antibody that corresponds to at least the EC₁₀₀, 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
15 (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 anti-NKG2A 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 EC₁₀₀, for NKG2A+ NK cell response.

20 28. Use according to any of Claims 25, 26 or 27, in which the EC₁₀₀ for NKG2A+ NK cell response is about 10 µg/ml.

29. Use according to any of Claims 25 to 28, in which anti-NKG2A antibody competes with HLA-E for binding to NKG2A.

30. Use of an anti-NKG2A antibody that binds and neutralizes the inhibitory activity of
25 NKG2A in the preparation of a medicament for the treatment of cancer in an individual, in which the anti-NKG2A 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 anti-NKG2A antibody is to be administered to the individual in an amount effective to achieve a blood concentration that corresponds to at least the EC₁₀₀, for NKG2A+ NK cell response.

31. Use according to Claim 30, in which the EC₁₀₀ for NKG2A+ NK cell response is about 10 µg/ml.
32. 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.