

CLAIMS

1. A compound that binds a human NKG2A polypeptide and neutralizes the inhibitory activity of NKG2A, for use in the treatment or prevention of a HNSCC in an individual.
2. A method according to Claim 1, in which the HNSCC is an OCSCC.
- 5 3. A method according to Claim 1, in which the HNSCC is an oropharyngeal tumor.
4. A method according to Claim 1, in which the HNSCC is a larynx tumor.
5. A method according to Claim 1, in which the HNSCC is a tumor of the hypopharynx.
6. A method according to any preceding claim, in which the individual is HPV positive.
7. A compound for use according to any preceding claim, in which the treatment or
10 prevention of a HNSCC in an individual comprises:
 - (a) determining whether an individual having a HNSCC is HPV positive, and
 - (b) upon a determination that the individual is HPV positive, administering to the individual the compound that binds a NKG2A polypeptide.
8. A compound for use according to any preceding claim, in which the treatment or
15 prevention of a HNSCC in an individual comprises:
 - (a) determining whether HLA-E polypeptide is expressed by malignant cells from the individual having a HNSCC, and
 - (b) upon a determination that malignant cells express HLA-E polypeptide at or above a reference level, administering to the individual a compound that neutralizes the
20 inhibitory activity of a human NKG2A polypeptide.
9. A compound for use according to Claim 8, in which determining whether HLA-E polypeptide is expressed by malignant cells comprises obtaining from the individual a biological sample that comprises HNSCC cells, bringing the cells into contact with an antibody that binds a HLA-E polypeptide, and detecting cells that express HLA-E.
- 25 10. A compound that binds a human NKG2A polypeptide and neutralizes the inhibitory activity of NKG2A, for use in a method for treatment or prevention of a cancer in an individual, in which the method comprises:

(a) determining the HLA-E polypeptide status of malignant cells from the individual having a cancer,

(b) determining the EGFR polypeptide status of malignant cells from the individual having a cancer and

5 (c) upon a determination that HLA-E and EGFR polypeptides are expressed by malignant cells from the individual at levels that are at or above a reference level, administering to the individual a therapeutic regimen that comprises a compound that neutralizes the inhibitory activity of a human NKG2A polypeptide an agent that binds EGFR.

10 11. A compound for use according to Claim 10, in which the individual has an advanced HNSCC.

12. A compound for use according to any of Claims 8 to 11, in which the compound that neutralizes the inhibitory activity of a human NKG2A polypeptide is administered to the individual upon a determination that malignant cells from the individual have increased HLA-
15 E polypeptide expression compared to a reference level corresponding to a healthy individual.

13. A compound that binds a human NKG2A polypeptide and neutralizes the inhibitory activity of NKG2A, for use in a method for treatment or prevention of a cancer in an individual, in which the method comprises:

20 (a) determining whether the individual has a cancer characterized by the presence of lymphocytes in the tumor environment; and

(b) upon a determination that the individual has a cancer characterized by the presence of lymphocytes in the tumor environment, administering to the individual a compound that neutralizes the inhibitory activity of a human NKG2A polypeptide.

14. A compound for use according to any preceding claim, in which the compound that
25 binds a NKG2A polypeptide is an anti-NKG2A antibody.

15. A compound for use according to Claim 14, in which the antibody comprises a human IgG4 constant region.

16. A compound for use according to Claim 14 or 15, in which the antibody comprises an Fc-engineered constant region comprising an amino acid modification that reduces binding to a human Fcγ receptor.

17. A compound for use according to Claim 14 or 15, in which the anti-NKG2A antibody competes with the antibodies having the heavy and light chains comprising of SEQ ID NOS: 2 and 7 respectively for binding to human NKG2A.

18. A compound for use according to any of Claims 14 to 17, in which the compound or NKG2A antibody comprises the CDR1, CDR2 and CDR3 domains of a heavy chain having the sequence set forth in SEQ ID NO: 2, and the CDR1, CDR2 and CDR3 domains of a light chain having the sequence set forth in SEQ ID NO: 7.

19. A compound for use according to any of Claims 14 to 18, in which the anti-NKG2A antibody is administered as a pharmaceutically acceptable composition comprising a therapeutically effective amount of the anti-NKG2A antibody.

20. A compound for use according to Claim 19, in which the composition is free of any other pharmaceutically active agents.

21. A compound for use according to any preceding claim, in which the anti-NKG2A antibody is administered several times at a dosing frequency from once about every week to once about per month.

22. A compound that binds a human NKG2A polypeptide and neutralizes the inhibitory activity of NKG2A, for use in method of treating a cancer in a human patient, the method comprising administering to the patient an effective amount of each of: (a) an antibody that neutralizes the inhibitory activity of human NKG2A, and (b) an agent that binds EGFR.

23. A compound for use according to Claim 22, in which the agent that binds EGFR inhibits the biological activity of EGFR.

24. A compound for use according to Claim 22 or 23, in which the agent that binds EGFR is an antibody that induces ADCC toward EGFR-expressing tumor cells.

25. A compound for use according to Claim 22 or 24, in which the agent that binds EGFR is cetuximab.

26. A compound for use according to any of Claims 22 to 25, in which the cancer is HNSCC.

27. A compound for use according to Claim 26, in which the HNSCC is an OCSCC.

28. A compound for use according to any of Claims 22 to 27, in which the method
5 comprises at least one administration cycle, in which the cycle is a period of two weeks, in which for each of the at least one cycles, one dose of the antibody that neutralizes the inhibitory activity of human NKG2A is administered and two doses of the antibody that binds EGFR are administered.

29. A compound for use according to any of Claims 22 to 28, in which the method
10 comprises at least one administration cycle, in which the cycle is a period of two weeks, in which for each of the at least one cycles, one dose of the antibody that neutralizes the inhibitory activity of human NKG2A are administered at a dose of 1-10 mg/kg and two doses of the antibody that binds EGFR are administered at a dose of 1-10 mg/kg.

CLAIMS

1. Use of an antibody that binds a human NKG2A polypeptide and neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for the treatment or prevention of a head and neck squamous cell carcinoma (HNSCC) in an individual.
- 5 2. Use according to Claim 1, in which the HNSCC is an oral cavity squamous cell carcinoma (OCSCC).
3. Use according to Claim 1, in which the HNSCC is an oropharyngeal tumor.
4. Use according to Claim 1, in which the HNSCC is a larynx tumor.
5. Use according to Claim 1, in which the HNSCC is a tumor of the hypopharynx.
- 10 6. Use according to Claim 1, in which the individual is HPV positive.
7. Use according to Claim 1, in which:
 - (a) a determination is made as to whether HLA-E polypeptide is expressed by malignant cells from the individual having a HNSCC, and
 - (b) upon a determination that malignant cells express HLA-E polypeptide at or above
15 a reference level, the antibody is to be administered to the individual.
8. Use according to Claim 7, in which determining whether HLA-E polypeptide is expressed by malignant cells comprises bringing HNSCC cells obtained from an individual into contact with an antibody that binds a HLA-E polypeptide, and detecting cells that express HLA-E.
- 20 9. Use according to Claim 1, in which the antibody comprises an Fc-engineered constant region comprising an amino acid modification that reduces binding to a human Fc γ receptor.
10. Use according to Claim 1, in which the anti-NKG2A antibody comprises the CDR1, CDR2 and CDR3 domains of a heavy chain having the sequence set forth in SEQ ID NO: 2, and the CDR1, CDR2 and CDR3 domains of a light chain having the sequence set forth in
25 SEQ ID NO: 7.
11. Use according to Claim 1, in which the anti-NKG2A antibody is administered several times at a dosing frequency from once about every week to once about per month.

12. Use of an antibody that binds a human NKG2A polypeptide and neutralizes the inhibitory activity of NKG2A in the preparation of a medicament for treating a cancer in a human patient, in which an effective amount of each of: (a) an antibody that neutralizes the inhibitory activity of human NKG2A, and (b) an agent that binds the epidermal growth factor receptor (EGFR) is to be administered to the patient.
13. Use according to Claim 12, in which the agent that binds EGFR inhibits the biological activity of EGFR.
14. Use according to Claim 12, in which the agent that binds EGFR is an antibody that induces ADCC toward EGFR-expressing tumor cells.
15. Use according to Claim 12, in which the agent that binds EGFR is cetuximab.
16. Use according to Claim 12, which comprises at least one administration cycle, in which the cycle is a period of two weeks, in which for each of the at least one cycles, one dose of the antibody that neutralizes the inhibitory activity of human NKG2A is to be administered and two doses of an antibody that binds EGFR are to be administered.
17. Use according to Claim 12, which comprises at least one administration cycle, in which the cycle is a period of two weeks, in which for each of the at least one cycles, one dose of the antibody that neutralizes the inhibitory activity of human NKG2A is to be administered at a dose of 1-10 mg/kg and two doses of an antibody that binds EGFR are to be administered at a dose of 1-10 mg/kg.
18. Use according to Claim 12, in which the agent that binds EGFR is cetuximab and the NKG2A antibody comprises the CDR1, CDR2, and CDR3 domains of a heavy chain having the sequence set forth in SEQ ID NO: 2 and the CDR1, CDR2 and CDR3 domains of a light chain having the sequence set forth in SEQ ID NO: 7.