Claims

1. A pharmaceutical combination comprising an antibody and at least bortezomib, wherein said antibody specifically recognizes CD38 and wherein said antibody is capable of killing a $CD38^+$ cell by apoptosis, antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytoxicity (CDC), and wherein said antibody comprises at least one heavy chain and at least one light chain, wherein

(i) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 1, 2, and 3, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 4, 5, and 6;

(ii) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 7, 8, and 9, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 10, 11, and 12;

(iii) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 13, 14 (or 81), and 15, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 16, 17, and 18;

(iv) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 19, 20, and 21, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 22, 23, and 24;

(v) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 25, 26, and 27, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 28, 29, and 30; or

(vi) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 31, 32, and 33, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 34, 35, and 36.

2. The combination of claim 1, wherein said antibody is a chimeric or humanized antibody.

3. The combination of claim 1 or 2 wherein said heavy chain comprises an amino acid sequence SEQ ID NO: 66 and wherein said light chain comprises an amino acid sequence selected from the group of SEQ ID NOS: 62 or 64.

4. The combination of claim 1 or 2 wherein said heavy chain comprises an amino acid sequence represented by SEQ ID NO: 72 and wherein said light chain comprises an amino acid sequence selected from the group of SEQ ID NOS: 68 and 70.

5. A pharmaceutical combination comprising an antibody and at least bortezomib, wherein said antibody specifically recognizes CD38 and wherein said antibody consists of:

- a light chain comprising an amino acid sequence of SEQ ID NOS: 62; and
- a heavy chain comprising an amino acid sequence of SEQ ID NO: 66.

6. The combination according to any one of claim 1 to 5 for use in the treatment of cancer, wherein the antitumor efficacy of the combination is from about 11 to about 42% T/C.

7. The combination according to any one of claims 1 to 5 for use in the treatment of cancer, wherein the antitumor efficacy of the combination is from about 0 to about 10% T/C.

8. A pharmaceutical combination according to any one of claims 1 to 7 for use in the treatment of cancer.

9. The combination according to any one of claims 6 to 8 wherein the antibody specifically recognizing CD38 and bortezomib are to be administered separately.

10. The combination according to any one of claim 6 to 8 wherein the antibody specifically recognizing CD38 and bortezomib are to be administered semi-simultaneously.

11. The combination according to any one of claims 6 to 9 wherein the antibody specifically recognizing CD38 and bortezomib are to be administered spaced out over a period of time so as to obtain the maximum efficacy of the combination.

12. An article of manufacture comprising:

a) a packaging material

b) a combination of an antibody and at least bortezomib, wherein said antibody specifically recognizes CD38 and wherein said antibody is capable of killing a $CD38^+$ cell by apoptosis, antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytoxicity (CDC), and wherein said antibody comprises at least one heavy chain and at least one light chain, wherein

(i) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 1, 2, and 3, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 4, 5, and 6;

(ii) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 7, 8, and 9, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 10, 11, and 12;

(iii) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 13, 14 (or 81), and 15, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 16, 17, and 18;

(iv) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 19, 20, and 21, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences

represented by SEQ ID NOS: 22, 23, and 24;

(v) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 25, 26, and 27, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 28, 29, and 30; or

(vi) said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 31, 32, and 33, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 34, 35, and 36, and

c) a label or package insert contained within said packaging material indicting that said combination thereof is effective for treating cancer.

Claims

1. A pharmaceutical combination comprising an antibody specifically recognizing CD38 and at least bortezomib, wherein said antibody is capable of killing a $CD38^+$ cell by apoptosis, antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytoxicity (CDC).

2. The combination of claim 1, wherein said antibody is a humanized antibody.

3. The combination of claim 2 wherein said antibody comprises one or more complementarity-determining region having an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36 and 81.

4. The combination of claim 3 wherein said antibody comprises at least one heavy chain and at least one light chain, wherein said heavy chain has an amino acid sequence SEQ ID NO: 66 and said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 13, 14 (or 81), and 15, and wherein said light chain amino acid sequence is SEQ ID NOS: 62 or 64, and said light chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 16, 17 and 18.

5. The combination of claim 3 wherein said antibody comprises at least one heavy chain and at least one light chain, wherein said heavy chain has an amino acid sequence represented by SEQ ID NO: 72 and said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 25, 26, and 27, and wherein said light chain has an amino acid sequence selected from the group of SEQ ID NOS: 68 and 70, and said light chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 28, 29, and 30.

6. The combination according to claim 1 for use in the treatment of cancer, wherein the antitumor efficacy of the combination is from about 11 to about 42% T/C.

7. The combination according to claim 1 for use in the treatment of cancer, wherein the antitumor efficacy of the combination is from about 0 to about 10% T/C.

8. A pharmaceutical combination according to claim 1 for use in the treatment of cancer.

9. The combination of claim 8, wherein said antibody is a humanized antibody.

10. The combination of claim 9 wherein said antibody comprises one or more complementarity-determining region having an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36 and 81.

11. The combination of claim 9 wherein said antibody comprises at least one heavy chain and at least one light chain, wherein said heavy chain has an amino acid sequence SEQ ID NO: 66 and said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 13, 14 (or 81), and 15, and wherein said light chain has an amino acid sequence selected from the group of SEQ ID NOS: 62 and 64, and said light chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 16, 17, and 18.

12. The combination of claim 11 wherein said antibody comprises at least one heavy chain and at least one light chain, wherein said heavy chain has an amino acid sequence SEQ ID NO: 72 and said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 25, 26, and 27, and wherein said light chain has an

amino acid sequence of SEQ ID NOS: 68 or 70, and said light chain comprises three sequential complementarity-determining regions having amino acid sequences SEQ ID NOS: 28, 29, and 30.

13. The combination according to claims 8 to 12 wherein the antibody specifically recognizing CD38 and bortezomib are administered separately.

14. The combination according to claims 8 to 12 wherein the antibody specifically recognizing CD38 and bortezomib are administered semi-simultaneously.

15. The combination according to claims 8 to 12 wherein the administration of antibody specifically recognizing CD38 and bortezomib are spaced out over a period of time so as to obtain the maximum efficacy of the combination.

16. An article of manufacture comprising:
a) a packaging material
b) a combination of an antibody specifically recognizing CD38 and at least bortezomib, wherein said antibody is capable of killing a $CD38^+$ cell by apoptosis, antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytoxicity (CDC), and
c) a label or package insert contained within said packaging material indicating that said combination thereof is effective for treating cancer.

17. The combination according to claims 8 to 15 wherein the cancer is a CD38 expressing cancer.

18. The combination according to claim 17 wherein the CD38 expressing cancer is a hematological cancer.

19. The combination according to claim 18 wherein the hematological cancer is selected from the group consisting of multiple myeloma, leukemia, acute and chronic lymphocytic leukemia, acute and chronic lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, non- Hodgkin lymphoma; acute and chronic myelogenous leukemias, and promyelocytic leukemia.