

Claims

1. Use of a bispecific antibody comprising a first binding part specifically binding to human B cell maturation antigen (BCMA) and a second binding part specifically binding to human CD3ε (CD3) and an immunotherapeutic drug selected from the group consisting of thalidomide or an immunotherapeutic derivative thereof, an anti-CD38 antibody, an anti-PD-1 antibody and an anti-PD-L1 antibody, in the manufacture of a medicament for treating multiple myeloma, wherein the first binding part comprises:
 - i) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L region of SEQ ID NO:20;
 - ii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20;
 - iii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20; or
 - iv) a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID NO:20.
2. The use according to claim 1, wherein the immunotherapeutic drug is daratumumab, isatuximab, MOR202, Ab79, Ab19, thalidomide, lenalidomide, pomalidomide, CC-122, CC220, pembrolizumab, pidilizumab, nivolumab, MEDI-0680, PDR001, REGN2810, lambrolizumab, MDX-1106, BGB-108, h409A11, h409A16, h409A17, atezolizumab, avelumab, durvalumab or MDX-1105.
3. The use according to claim 1 or 2, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L

region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L region of SEQ ID NO:20.

4. The use according to claim 1 or 2, wherein the first binding part of the bispecific antibody
5 comprises a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20.

10 5. The use according to claim 1 or 2, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20.

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6. The use according to claim 1 or 2, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID
20 NO:20.

7. A therapeutic combination for achieving multiple myeloma cell lysis in a patient suffering from multiple myeloma disease, wherein the combination comprises a therapeutically effective amount of:

25 a) a bispecific antibody comprising a first binding part specifically binding to human B cell maturation antigen (BCMA) and a second binding part specifically binding to human CD3ε (CD3); and

b) an immunotherapeutic drug selected from the group consisting of thalidomide or an immunotherapeutic derivative thereof, an anti-CD38 antibody, an anti-PD-1 antibody and an anti-
30 PD-L1 antibody,

wherein the first binding part comprises:

i) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L
35 region of SEQ ID NO:20;

- ii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20;
- 5 iii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20; or
- 10 iv) a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID NO:20.
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8. An article of manufacture, comprising
- 15 a) a bispecific antibody comprising a first binding part specifically binding to human B cell maturation antigen (BCMA) and a second binding part specifically binding to human CD3ε (CD3), wherein the first binding part comprises:
- 20 i) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L region of SEQ ID NO:20;
- 25 ii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20;
- 30 iii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20; or
- 30 iv) a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID NO:20;
- b) an immunotherapeutic drug selected from the group consisting of thalidomide or an immunotherapeutic derivative thereof, an anti-CD38 antibody, an anti-PD-1 antibody and an anti-PD-L1 antibody; and

c) a pharmaceutically acceptable carrier and instructions for administering the bispecific antibody and the immunotherapeutic drug in combination to a subject in need of a treatment for multiple myeloma.

9. A method for manufacturing a medicament, wherein the method comprises using a therapeutically effective amount of

a) a bispecific antibody comprising a first binding part specifically binding to human B cell maturation antigen (BCMA) and a second binding part specifically binding to human CD3 ϵ (CD3), wherein the first binding part comprises:

i) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L region of SEQ ID NO:20;

ii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20;

iii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20; or

iv) a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID NO:20; and

b) an immunotherapeutic drug selected from the group consisting of thalidomide or an immunotherapeutic derivative thereof, an anti-CD38 antibody, an anti-PD-1 antibody and an anti-PD-L1 antibody, and combining the bispecific antibody and the immunotherapeutic drug in a pharmaceutically acceptable carrier.

10. A kit comprising:

a) a pharmaceutical composition comprising a bispecific antibody comprising a first binding part specifically binding to human B cell maturation antigen (BCMA) and a second binding part specifically binding to human CD3 ϵ (CD3), wherein the first binding part comprises:

i) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L region of SEQ ID NO:20;

- ii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20;
- 5 iii) a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20; or
- 10 iv) a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID NO:20; and
- b) a pharmaceutical composition comprising an immunotherapeutic drug selected from the group consisting of thalidomide or an immunotherapeutic derivative thereof, an anti-CD38
- 15 antibody, an anti-PD-1 antibody and an anti-PD-L1 antibody.

11. The therapeutic combination according to claim 7, the article of manufacture according to claim 8, the method for manufacturing a medicament according to claim 9, or the kit according to claim 10, wherein the immunotherapeutic drug is daratumumab, isatuximab, MOR202, Ab79,

20 Ab19, thalidomide, lenalidomide, pomalidomide, CC-122, CC-220, pembrolizumab, pidilizumab, nivolumab, MEDI-0680, PDR001, REGN2810, lambrolizumab, MDX-1106, BGB-108, h409A11, h409A16, h409A17, atezolizumab, avelumab, durvalumab, or MDX-1105.

12. The therapeutic combination according to claim 7 or 11, the article of manufacture according to claim 8 or 11, the method for manufacturing a medicament according to claim 9 or 11, or the

25 kit according to claim 10 or 11, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:27, a CDR2L region of SEQ ID NO:28 and a CDR3L region of SEQ ID NO:20.

30 13. The therapeutic combination according to claim 7 or 11, the article of manufacture according to claim 8 or 11, the method for manufacturing a medicament according to claim 9 or 11, or the kit according to claim 10 or 11, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID

35 NO:25, a CDR2L region of SEQ ID NO:26 and a CDR3L region of SEQ ID NO:20.

14. The therapeutic combination according to claim 7 or 11, the article of manufacture according to claim 8 or 11, the method for manufacturing a medicament according to claim 9 or 11, or the kit according to claim 10 or 11, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:21, a CDR2H region of SEQ ID NO:22
5 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:23, a CDR2L region of SEQ ID NO:24 and a CDR3L region of SEQ ID NO:20.

15. The therapeutic combination according to claim 7 or 11, the article of manufacture according to claim 8 or 11, the method for manufacturing a medicament according to claim 9 or 11, or the
10 kit according to claim 10 or 11, wherein the first binding part of the bispecific antibody comprises a VH region comprising a CDR1H region of SEQ ID NO:15, a CDR2H region of SEQ ID NO:16 and a CDR3H region of SEQ ID NO:17 and a VL region comprising a CDR1L region of SEQ ID NO:18, a CDR2L region of SEQ ID NO:19, and a CDR3L region of SEQ ID NO:20.

16. The use according to any one of claims 1-6, wherein the bispecific antibody and the
15 immunotherapeutic drug are administered by different administration routes or are administered according to different treatment schedules.

17. The use according to any one of claims 1-6, wherein the bispecific antibody and the immunotherapeutic drug are administered together.