

CLAIMS

1. Use of a BCMAxCD3 bispecific antibody for the manufacture of a medicament for treating a cancer in a subject in need thereof, wherein the BCMAxCD3 bispecific antibody is to be administered in combination with an anti-CD38 antibody, comprising:
 - (1) a BCMAxCD3 bispecific antibody to be administered to the subject at a dose of 200 µg/kg to 6 mg/kg or 60 mg to 600 mg every 1-4 weeks, and
 - (2) an anti-CD38 antibody to be administered to the subject at a dose of 1200 mg to 2400 mg every 1-4 weeks.
2. The use of claim 1, comprising:
 - (1) the BCMAxCD3 bispecific antibody to be subcutaneously administered at a dose of 1 mg/kg to 6 mg/kg or 60 mg to 600 mg every 1-4 weeks, and
 - (2) the anti-CD38 antibody to be subcutaneously administered at a dose of 1600 mg to 2000 mg every 1-4 weeks.
3. The use of claim 2, further comprising the BCMAxCD3 bispecific antibody to be subcutaneously administered at a dose lower than 0.5 mg/kg prior to step (1).
4. The use of claim 2 or claim 3, wherein the BCMAxCD3 bispecific antibody is to be subcutaneously administered to the subject at a dose of 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 5, 5.5, or 6 mg/kg, or 60, 100, 150, 200, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600 mg, or any dose from about 1 mg to about 600 mg, once every week or once every two weeks.
5. The use of claim 4, wherein the BCMAxCD3 bispecific antibody is to be subcutaneously administered to the subject at a dose of 1.5 mg/kg weekly, 3.0 mg/kg weekly or biweekly, 6.0 mg/kg monthly, 60-150 mg weekly, 150-300 mg biweekly, or 300-600 mg monthly.

6. The use of claim 5, wherein the BCMAxCD3 bispecific antibody is to be subcutaneously administered to the subject at a dose of 1.5 mg/kg or 60-150 mg weekly.
7. The use of claim 5, wherein the BCMAxCD3 bispecific antibody is to be subcutaneously administered to the subject at a dose of 3 mg/kg or 150-300 mg biweekly.
8. The use of claim 5, wherein the BCMAxCD3 bispecific antibody is to be subcutaneously administered to the subject at a dose of 6 mg/kg or 300-600 mg monthly.
9. The use of any one of claims 1-8, wherein the anti-CD38 antibody is to be subcutaneously administered to the subject in the dose of 1800 mg once every week during week 1 to week 8 of the treatment, once every two weeks during week 9 to week 24 of the treatment, and once every four weeks after week 24 of the treatment.
10. The use of any one of claims 1-9, wherein the anti-CD38 antibody is to be administered or provided for administration together with rHuPH20, such as about 30,000 U of rHuPH20.
11. The use of any one of claims 1-10, wherein the BCMAxCD3 bispecific antibody comprises:
 - (1) a BCMA binding domain comprising a heavy chain variable region (VH) having heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3 of the amino acid sequences of SEQ ID NO: 18, SEQ ID NO: 19, and SEQ ID NO: 20, respectively, and a light chain variable region (VL) having light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3 of the amino acid sequences of SEQ ID NO: 21, SEQ ID NO: 22, and SEQ ID NO: 23, respectively, and
 - (2) a CD3 binding domain comprising a VH having HCDR1, HCDR2 and HCDR3 of the amino acid sequences of SEQ ID NO: 28, SEQ ID NO:

29, and SEQ ID NO: 30, respectively, and a VL having LCDR1, LCDR2 and LCDR3 of the amino acid sequences of SEQ ID NO: 31, SEQ ID NO: 32, and SEQ ID NO: 33, respectively.

12. The use of claim 11, wherein the BCMA binding domain comprises the VH having the amino acid sequence of SEQ ID NO: 24 and the VL having the amino acid sequence of SEQ ID NO: 25; the CD3 binding domain comprises the VH having the amino acid sequence of SEQ ID NO: 34 and the VL having the amino acid sequence of SEQ ID NO: 35.
13. The use of claim 10, wherein the BCMAxCD3 bispecific antibody comprises a first heavy chain (HC1) having the amino acid sequence of SEQ ID NO: 26, a first light chain (LC1) having the amino acid sequence of SEQ ID NO: 27, a second heavy chain (HC2) having the amino acid sequence of SEQ ID NO: 36, and a second light chain (LC2) having the amino acid sequence of SEQ ID NO: 37.
14. The use of any one of claims 1-13, wherein the anti-CD38 antibody comprises a VH having HCDR1, HCDR2 and HCDR3 of the amino acid sequences of SEQ ID NO: 8, SEQ ID NO: 9, and SEQ ID NO: 10, respectively, and a VL having LCDR1, LCDR2 and LCDR3 of the amino acid sequences of SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13, respectively.
15. The use of claim 14, wherein the CD38 antibody comprises the VH having the amino acid sequence of SEQ ID NO: 6, and the VL having the amino acid sequence of SEQ ID NO: 7.
16. The use of any one of claims 1-15, wherein the cancer is multiple myeloma.
17. Use of a BCMAxCD3 bispecific antibody for the manufacture of a medicament for treating multiple myeloma in a subject in need thereof, wherein the BCMAxCD3 bispecific antibody is to be administered in combination with an anti-CD38 antibody, comprising:
 - (i) 1.5 mg/kg of a BCMAxCD3 bispecific antibody once every week during week 1 to week 8 of the treatment, and 3.0 mg/kg of the BCMAxCD3

bispecific antibody once every two weeks and/or 6.0 mg/kg of a BCMAxCD3 bispecific antibody once every month after week 8 of the treatment to be subcutaneously administered to the subject, and

- (ii) 1800 mg of an anti-CD38 antibody once every week during week 1 to week 8 of the treatment, once every two weeks during week 9 to week 24 of the treatment, and once every four weeks after week 24 of the treatment to be subcutaneously administered to the subject,

wherein the BCMAxCD3 bispecific antibody comprises a first heavy chain (HC1) of SEQ ID NO: 26, a first light chain (LC1) of SEQ ID NO: 27, a second heavy chain (HC2) of SEQ ID NO: 36, and a second light chain (LC2) of SEQ ID NO: 37, and the anti-CD38 antibody comprises the HC of SEQ ID NO: 14 and the LC of SEQ ID NO: 15.

18. The use of claim 17, further comprising 0.06 mg/kg of the BCMAxCD3 bispecific antibody to be subcutaneously administered to the subject on Day 2 of the treatment and 0.3 mg/kg of the BCMAxCD3 bispecific antibody to be subcutaneously administered to the subject on Day 4 of the treatment, prior to the initial subcutaneous administration of the 1.5 mg/kg BCMAxCD3 bispecific antibody.
19. The use of any one of claims 1-18, wherein the subject has received at least one prior treatment for multiple myeloma, or the subject is relapsed or refractory to the at least one prior treatment, wherein the prior treatment can comprise at least one of a proteasome inhibitor (PI) or an immunomodulatory agent (IMiD).
20. The use of claim 16, wherein the subject is refractory or relapsed to a treatment selected from the group consisting of an anti-CD38 antibody, lenalidomide, bortezomib, pomalidomide, carfilzomib, elotuzumab, ixazomib, isatuximab, melphalan and thalidomide, or any combination thereof, preferably, the subject is lenalidomide refractory.
21. The use of any one of claims 1-20, further comprising an additional therapeutic to be administered to the subject, such as pomalidomide and/or dexamethasone.

22. The use of any one of claims 1-21, wherein the treatment results in T-cell activation, such as an increase in at least one of CD25, PD-1, CD38 on CD4 and CD8 T cells, or the treatment results in an increase in frequency of at least of CD38+ CD8+ T cells, CD38+ CD4+ T cells and Tregs T cells.