

Claims

- 1) The use of an anti-CD38 antibody in the manufacture of a medicament for the treatment of refractory or relapsed acute myeloid leukemia (AML), wherein the anti-CD38 antibody comprises the heavy chain complementarity determining regions (HCDR): 1 (HCDR1), 2 (HCDR2) and 3 (HCDR3) sequences of SEQ ID NOs: 6, 7 and 8, respectively, and the light chain complementarity determining regions (LCDR): 1 (LCDR1), 2 (LCDR2) and 3 (LCDR3) sequences of SEQ ID NOs: 9, 10 and 11, respectively.
- 2) The use of claim 1, wherein the anti-CD38 antibody induces killing of AML cells that express CD38 by apoptosis.
- 3) The use of claim 1 or 2, wherein the anti-CD38 antibody is of IgG1, IgG2, IgG3 or IgG4 isotype.
- 4) The use of claims 1 or 2, wherein the anti-CD38 antibody comprises the heavy chain variable region (VH) of SEQ ID NO: 4 and the light chain variable region (VL) of SEQ ID NO: 5.
- 5) The use of claims 1 or 2, wherein the anti-CD38 antibody comprises the heavy chain of SEQ ID NO: 12 and the light chain of SEQ ID NO: 13.
- 6) The use of any one of claims 2, 4 or 5, wherein AML is AML with at least one genetic abnormality.
- 7) The use of claim 6, wherein the at least one genetic abnormality is a mutation in a gene selected from the group consisting of fms-related tyrosine kinase 3 (FLT3), nucleophosmin (NPM1), isocitrate dehydrogenase 1 (IDH1), isocitrate dehydrogenase 2 (IDH2), DNA (cytosine-5)-methyltransferase 3 (DNMT3A), or CCAAT/enhancer binding protein alpha (CEBPA).

8) The use of claim 7, wherein the mutation in FLT3 is FLT3-ITD, the mutations in IDH2 is R140Q or the mutation in DNMT3A is R882H.

9) The use of any one of claims 1-8, wherein the anti-CD38 antibody is to be administered in combination with at least one second therapeutic agent.

10) The use of claim 9, wherein the at least one second therapeutic agent is cytarabine, daunorubicin, idarubicin, mitoxantrone, hydroxyurea, decitabine, cladribine, fludarabine, topotecan, etoposide 6-thioguanine, corticosteroid, prednisone, dexamethasone, methotrexate, 6-mercaptopurine, azacitidine, arsenic trioxide or all-trans retinoic acid.

11) The use of claim 9, wherein the at least one second therapeutic agent is all-trans retinoic acid, cytarabine, decitabine or doxorubicin.

12) The use of any of the claims 9-11, wherein the anti-CD38 antibody and the at least one second therapeutic agent are administered simultaneously, sequentially or separately.

13) The use of any of the claims 9-12, wherein the at least one second therapeutic agent increases surface expression of CD38 on AML cells.

14) The use of any one of claims 1-13, wherein the subject is further treated or has been treated with radiotherapy.

15) The use of any one of claims 1-14, wherein the subject is undergoing hematopoietic stem cell transplantation (HSCT).

16) The use of claim 15, wherein the HSCT is allogeneic, autologous or syngeneic.

17) The use of claim 15, wherein the HSCT comprises transplantation of blood stem cells derived from bone marrow, blood or amniotic fluid.

18) The use of any of the claims 1-8, further wherein the subject has been treated with idarubicin, cytarabine or hydroxyurea.