

Claims

- 1) An anti-CD38 antibody for use in the treatment of acute myeloid leukemia (AML).
- 2) The use of an anti-CD38 antibody in the manufacture of a medicament for the treatment of myeloid leukemia(AML)
- 3) The anti-CD38 antibody of claim 1 or the use of claim 2, wherein the anti-CD38 antibody competes for binding to human CD38 of SEQ ID NO: 1 with an antibody comprising a heavy chain variable region (VH) of SEQ ID NO: 4 and a light chain variable region (VL) of SEQ ID NO: 5.
- 4) The anti-CD38 antibody of claim 1 or 3 or the use of claim 2 or claim 3, wherein the anti-CD38 antibody binds to the region SKRNIQFSCCKNIYR (SEQ ID NO: 2) and the region EKVQTLEAWVIHGG (SEQ ID NO: 3) of human CD38 (SEQ ID NO: 1).
- 5) The anti-CD38 antibody of any of the claims 1, 3 or 4, or the use of any one of claims 2-4, wherein the anti-CD38 antibody induces killing of AML cells that express CD38 by apoptosis.
- 6) The anti-CD38 antibody of claim 1 or any of the claims 3-5, or the use of any one of claims 2-5, wherein the anti-CD38 antibody is of IgG1, IgG2, IgG3 or IgG4 isotype.
- 7) The anti-CD38 antibody of claim 1 or any of the claims 3-6, or the use of any one of claims 2-6, 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.
- 8) The anti-CD38 antibody or the use of claim 7, 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.
- 9) The anti-CD38 antibody or the use of claim 8, wherein the anti-CD38 antibody comprises the heavy chain of SEQ ID NO: 12 and the light chain of SEQ ID NO: 13.
- 10) The anti-CD38 antibody of claim 1 or any of the claims 3-6, or the use of any one of claims 2-6, wherein the anti-CD38 antibody comprises the VH and the VL of SEQ ID NOs: 15 and 16, respectively.
- 11) The anti-CD38 antibody of claim 1 or any of the claims 3-6, or the use of any one of claims 2-6, wherein the anti-CD38 antibody comprises the VH and the VL of SEQ ID NOs: 17 and 18, respectively.
- 12) The anti-CD38 antibody of claim 1 or any of the claims 3-6, or the use of any one of claims 2-6, wherein the anti-CD38 antibody comprises the VH and the VL of SEQ ID NOs: 19 and 20, respectively.

- 13) The anti-CD38 antibody of claim 1 or any of the claims 3-6, or the use of any one of claims 2-6, wherein the anti-CD38 antibody comprises the VH and the VL of SEQ ID NOs: 21 and 22, respectively.
- 14) The anti-CD38 antibody of claim 1 or any of the claims 3-13, or the use of any one of claims 2-13, wherein AML is AML with at least one genetic abnormality, AML with multilineage dysplasia, therapy-related AML, undifferentiated AML, AML with minimal maturation, AML with maturation, acute myelomonocytic leukemia, acute monocytic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia, acute basophilic leukemia, acute panmyelosis with fibrosis or myeloid sarcoma.
- 15) The anti-CD38 antibody or the use of claim 14, wherein the at least one genetic abnormality is a translocation between chromosomes 8 and 21, a translocation or an inversion in chromosome 16, a translocation between chromosomes 15 and 17, changes in chromosome 11, or mutation in fms-related tyrosine kinase 3 (FLT3), nucleophosmin (NPM1), isocitrate dehydrogenase 1 (IDH1), isocitrate dehydrogenase 2 (IDH2), DNA (cytosine-5)-methyltransferase 3 (DNMT3A), CCAAT/enhancer binding protein alpha (CEBPA), U2 small nuclear RNA auxiliary factor 1 (U2AF1), enhancer of zeste 2 polycomb repressive complex 2 subunit (EZH2), structural maintenance of chromosomes 1A (SMC1A) or structural maintenance of chromosomes 3 (SMC3).
- 16) The anti-CD38 antibody or the use of claim 14, wherein the at least one genetic abnormality is a translocation t(8; 21)(q22; q22), an inversion inv(16)(p13; q22), a translocation t(16; 16)(p13; q22), a translocation t(15; 17)(q22; q12), a mutation FLT3-ITD, mutations R132H or R100Q/R104V/F108L/R119Q/I130V in IDH1 or mutations R140Q or R172 in IDH2.
- 17) The anti-CD38 antibody of claim 1 or any of the claims 3-16, or the use of any one of claims 2-16, wherein AML is refractory or relapsed.
- 18) The anti-CD38 antibody of claim 1 or any of the claims 3-17, or the use of any one of claims 2-17, wherein the anti-CD38 antibody is administered as a remission induction, post-remission or maintenance therapy.
- 19) The anti-CD38 antibody of claim 1 or any of the claims 3-18, or the use of any one of claims 2-18, wherein the anti-CD38 antibody is to be administered in combination with at least one second therapeutic agent.
- 20) The anti-CD38 antibody or the use of claim 19, 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.
- 21) The anti-CD38 antibody or the use of claim 19, wherein the at least one second therapeutic agent is all-trans retinoic acid, cytarabine, decitabine or doxorubicin.

- 22) The anti-CD38 antibody or the use of any of the claims 18-21, wherein the anti-CD38 antibody and the at least one second therapeutic agent are administered simultaneously, sequentially or separately.
- 23) The anti-CD38 antibody or the use of any of the claims 18-22, wherein the at least one second therapeutic agent increases surface expression of CD38 on AML cells.
- 24) The anti-CD38 antibody of claim 1 or any of the claims 3-23, or the use of any one of claims 2-23, wherein the subject is further treated or has been treated with radiotherapy.
- 25) The anti-CD38 antibody of claim 1 or any of the claims 3-24, or the use of any one of claims 2-24, wherein the subject is undergoing hematopoietic stem cell transplantation (HSCT).
- 26) The anti-CD38 antibody or the use of claim 25, wherein the HSCT is allogeneic, autologous or syngeneic.
- 27) The anti-CD38 antibody or the use of claim 26, wherein the HSCT comprises transplantation of blood stem cells derived from bone marrow, blood or amniotic fluid.