

Claims

1. A therapeutic agent directed against CD19 for use in the treatment of cancer in a patient, wherein the patient is refractory or relapsed from previous treatment, the previous treatment comprising an anti-CD19 antibody comprising an HCDR1 region comprising sequence SYVMH (SEQ ID NO: 1), an HCDR2 region comprising sequence NPYNDG (SEQ ID NO: 2), an HCDR3 region comprising sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDR1 region comprising sequence RSSKSLQNVNGNTYLY (SEQ ID NO: 4), an LCDR2 region comprising sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region comprising sequence MQHLEYPIT (SEQ ID NO: 6).
2. A therapeutic agent directed against CD19 for use according to any of the preceding claims, wherein the therapeutic agent is selected from the group of an antibody, an antibody-drug conjugate, a bispecific, an alternative scaffold protein or a chimeric antigen receptor (CAR) T cell.
3. A therapeutic agent directed against CD19 for use according to claim 2, wherein the therapeutic agent is a chimeric antigen receptor (CAR) T cell.
4. A chimeric antigen receptor (CAR) T cell directed against CD19 for use according to claim 3, wherein the CAR-T cell is axicabtagene ciloleucel, tisagenlecleucel, lisocabtagene maraleucel, or UCART19.
5. A therapeutic agent directed against CD19 for use according to any of the preceding claims, wherein the cancer is hematological cancer and selected from non-Hodgkin's B cell lymphoma, follicular lymphoma (FL), small lymphocytic lymphoma (SLL), Burkitt lymphoma, diffuse large B-cell lymphoma (DLBCL), Waldenstrom's macroglobulinemia, B cell leukemia, chronic lymphocytic leukemia (CLL), or acute lymphoblastic leukemia (ALL).
6. A therapeutic agent directed against CD19 for use according to claim 5, wherein the hematological cancer is relapsed or refractory hematological cancer.

7. A therapeutic agent directed against CD19 for use according to claim 6, wherein the relapsed or refractory hematological cancer is R/R - DLBCL.
8. An anti-CD19 antibody for use in the treatment of cancer in a patient, wherein said patient after such anti-CD19 antibody treatment is treated with a chimeric antigen receptor (CAR) T cell directed against CD19 and wherein the anti-CD19 antibody comprises an HCDR1 region comprising sequence SYVMH (SEQ ID NO: 1), an HCDR2 region comprising sequence NPYNDG (SEQ ID NO: 2), an HCDR3 region comprising sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDR1 region comprising sequence RSSKSLQNVNGNTYLY (SEQ ID NO: 4), an LCDR2 region comprising sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region comprising sequence MQHLEYPIT (SEQ ID NO: 6).
9. A sequential therapeutic combination comprising an anti-CD19 antibody and a chimeric antigen receptor (CAR) T cell directed against CD19 for use in the treatment of cancer.
10. The sequential therapeutic combination according to claim 9 for use in the treatment of cancer wherein the anti-CD19 antibody is administered to a cancer patient and wherein after said patient has relapsed or is refractory, a CAR-T cell directed against CD19 is administered to the patient.
11. The sequential therapeutic combination according to claim 10 for use in the treatment of cancer wherein the anti-CD19 antibody is administered in combination with one or more additional pharmaceutical agent.
12. The sequential therapeutic combination according to claim 11 for use in the treatment of cancer wherein said pharmaceutical agent is a therapeutic antibody or antibody fragment, a nitrogen mustard, a purine analog, a thalidomide analog, a phosphoinositide 3-kinase inhibitor, a BCL-2 inhibitor, a bruton's tyrosine kinase (BTK) inhibitor or a pharmaceutically acceptable salt thereof.
13. The sequential therapeutic combination according to claim 12 for use in the treatment of cancer, wherein the pharmaceutical agent is lenalidomide or a pharmaceutically acceptable salt thereof.

14. The sequential therapeutic combination according to claim 13 for use in the treatment of cancer, wherein said anti-CD19 antibody is administered in a regimen of up to 12 cycles wherein for cycles 1 to 3, said anti-CD19 antibody is administered weekly and from cycle 4 onwards, said anti-CD19 antibody is administered every 14 days and wherein
5 lenalidomide is administered daily.

15. A sequential therapeutic combination according to any one of the claims 9 to 14 wherein the anti-CD19 antibody comprises an HCDR1 region comprising sequence SYVMH (SEQ ID NO: 1), an HCDR2 region comprising sequence NPYNDG (SEQ ID NO: 2), an
10 HCDR3 region comprising sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDR1 region comprising sequence RSSKSLQNVNGNTYLY (SEQ ID NO: 4), an LCDR2 region comprising sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region comprising sequence MQHLEYPIT (SEQ ID NO: 6).

15

20

25

30