Claims

1. Use of an anti-CD19 antibody in the manufacture of a medicament for the treatment of a hematological cancer in a human subject, wherein the human subject has a peripheral NK cell count at baseline of less than 50 NK cells/µl, wherein the anti-CD19 antibody comprises an HCDR1 region comprising the sequence SYVMH (SEQ ID NO: 1), an HCDR2 region comprising the sequence NPYNDG (SEQ ID NO: 2), an HCDR3 region comprising the sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDR1 region comprising the sequence RSSKSLQNVNGNTYLY (SEQ ID NO: 4), an LCDR2 region comprising the sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region comprising the sequence MQHLEYPIT (SEQ ID NO: 6), and wherein the anti-CD19 antibody comprises a heavy chain constant region comprising amino acids 239D and 332E, wherein the Fc numbering is according to the EU index as in Kabat.

2. The use according to claim 1, wherein the hematological cancer is resistant, non-responsive or inadequately responsive to treatment by an anti-CD20 targeting therapy.

3. The use according to claim 2, wherein the anti-CD20 targeting therapy is rituximab.

4. The use according to any one of claims 1 to 3, wherein the anti-CD19 antibody comprises a variable heavy chain of the sequence
EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGKGLEWIGYINPYND
GTKYNEKFQGRVTISSDKSISTAYMELSSLRSEDTAMYYCARGTYYYGTRVFDYWG
QGTLVTVSS (SEQ ID NO: 7)
and a variable light chain of the sequence
DIVMTQSPATLSLSPGERATLSCRSSKSLQNVNGNTYLYWFQQKPGQSPQLLIYRMS
NLNSGVPDRFSGSGSGTEFTLTISSLEPEDFAVYYCMQHLEYPITFGAGTKLEIK (SEQ ID NO: 8).

5. The use according to any one of claims 1 to 3, wherein the anti-CD19 antibody comprises a heavy chain having the sequence
EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGKGLEWIGYINPYND
GTKYNEKFQGRVTISSDKSISTAYMELSSLRSEDTAMYYCARGTYYYGTRVFDYWG

QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS
GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK
THTCPPCPAPELLGGPDVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYV
DGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKALPAPEEK
TISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 11)
and a light chain having the sequence
DIVMTQSPATLSLSPGERATLSCRSSKSLQNVNGNTYLYWFQQKPGQSPQLLIYRMS
NLNSGVPDRFSGSGSGTEFTLTISSLEPEDFAVYYCMQHLEYPITFGAGTKLEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS
KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:
12).

6. The use according to any one of claims 1 to 5, wherein said anti-CD19 antibody is to be administered in combination with one or more additional pharmaceutical agent.

7. The use according to claim 6, wherein said one or more additional pharmaceutical agent is a biologic or a chemotherapeutic agent or a pharmaceutically acceptable salt thereof.

8. The use according to claim 6, wherein said one or more additional 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.

9. The use according to claim 6, wherein said one or more additional pharmaceutical agent is rituximab, R-CHOP, cyclophosphamide, chlorambucil, uramustine, ifosfamide, melphalan, bendamustine, mercaptopurine, azathioprine, thioguanine, fludarabine, thalidomide, lenalidomide, pomalidomide, idelalisib, duvelisib, copanlisib, ibrutinib, venetoclax or a pharmaceutically acceptable salt thereof.

10. The use according to any one of claims 1 to 9, wherein said hematologic cancer is a non-Hodgkin's lymphoma.

11. The use according to claim 10, wherein the non-Hodgkin’s lymphoma is selected from the group consisting of follicular lymphoma, small lymphocytic lymphoma, mucosa-associated lymphoid tissue lymphoma, marginal zone lymphoma, diffuse large B cell lymphoma, Burkitt's lymphoma and mantle cell lymphoma.

12. The use according to claim 10, wherein the non-Hodgkin’s lymphoma is Relapsed or Refractory Diffuse Large B-cell Lymphoma (r-r DLBCL).

13. The use according to any one of claims 1 to 9, wherein said hematologic cancer is chronic lymphocytic leukemia.

14. The use according to any one of claims 1 to 9, wherein said hematologic cancer is acute lymphoblastic leukemia.

15. A method of selecting a hematological cancer patient who is predicted to benefit from the therapeutic administration of an anti-CD19 antibody, said method comprising the following steps:
a) providing a blood sample obtained from said patient prior to treatment with said anti-CD19 antibody,
b) determining the peripheral NK cell count in the blood sample, and
c) selecting the patient on the basis that the patient has a peripheral NK cell count at baseline of less than 50 NK cells/µl,
wherein the anti-CD19 antibody comprises an HCDR1 region comprising the sequence SYVMH (SEQ ID NO: 1), an HCDR2 region comprising the sequence NPYNDG (SEQ ID NO: 2), an HCDR3 region comprising the sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDR1 region comprising the sequence RSSKSLQNVNGNTYLY (SEQ ID NO: 4), an LCDR2 region comprising the sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region comprising the sequence MQHLEYPIT (SEQ ID NO: 6), and wherein the anti-CD19 antibody comprises a heavy chain constant region comprising amino acids 239D and 332E, wherein the Fc numbering is according to the EU index as in Kabat.

16. The method according to claim 15, wherein the anti-CD19 antibody comprises a variable heavy chain of the sequence

EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGKGLEWIGYINPYND GTKYNEKFQGRVTISSDKSISTAYMELSSLRSEDTAMYYCARGTYYYGTRVFDYWG QGTLVTVSS (SEQ ID NO: 7)
and a variable light chain of the sequence
DIVMTQSPATLSLSPGERATLSCRSSKSLQNVNGNTYLYWFQQKPGQSPQLLIYRMS NLNSGVPDRFSGSGSGTEFTLTISSLEPEDFAVYYCMQHLEYPITFGAGTKLEIK (SEQ ID NO: 8).

17. The method according to claim 15, wherein the anti-CD19 antibody comprises a heavy chain having the sequence
EVQLVESGGGLVKPGGSLKLSCAASGYTFTSYVMHWVRQAPGKGLEWIGYINPYND GTKYNEKFQGRVTISSDKSISTAYMELSSLRSEDTAMYYCARGTYYYGTRVFDYWG QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDK THTCPPCPAPELLGGPDVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYV DGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKALPAPEEK TISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 11)
and a light chain having the sequence
DIVMTQSPATLSLSPGERATLSCRSSKSLQNVNGNTYLYWFQQKPGQSPQLLIYRMS NLNSGVPDRFSGSGSGTEFTLTISSLEPEDFAVYYCMQHLEYPITFGAGTKLEIKRTVA APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 12).

18. The method according to any one of claims 15 to 17, wherein said hematologic cancer is a non-Hodgkin's lymphoma.

19. The method according to claim 18, wherein the non-Hodgkin’s lymphoma is selected from the group consisting of follicular lymphoma, small lymphocytic lymphoma, mucosa-associated lymphoid tissue lymphoma, marginal zone lymphoma, diffuse large B cell lymphoma, Burkitt's lymphoma and mantle cell lymphoma.

20. The method according to claim 18, wherein the non-Hodgkin's lymphoma is Relapsed or Refractory Diffuse Large B-cell Lymphoma (r-r DLBCL).

21. The method according to any one of claims 15 to 17, wherein said hematologic cancer is chronic lymphocytic leukemia.

22. The method according to any one of claims 15 to 17, wherein said hematologic cancer is acute lymphoblastic leukemia.