

SUMMARY

The disclosure provides anti-human CD19 antibodies with high affinity.

5 The disclosure provides an antibody, that specifically binds to human CD19 with a higher affinity than an antibody comprising a variable heavy chain comprising an amino acid sequence of SEQ ID NO:113 and a variable light chain comprising an amino acid sequence of SEQ ID NO:114.

The disclosure provides an antibody that specifically binds to human CD19, wherein the antibody comprises

- 10 (a) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 43,
- (b) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 44,
- (c) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 45,
- (d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 46,
- (e) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 47, and
- (f) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 48.

15 In an embodiment, the antibody is a monoclonal antibody. In another embodiment, the antibody is a human, humanized or chimeric antibody. In another embodiment, the antibody is an antibody fragment that specifically binds to human CD19.

In one aspect, there is provided an antibody that specifically binds to human CD19, wherein the antibody comprises a VH domain comprising an amino acid sequence of SEQ ID
20 NO: 99 and a VL domain comprising an amino acid sequence of SEQ ID NO: 100.

In a further embodiment, provided is an antibody as described herein before, which is a full length IgG1 antibody.

In a particular embodiment, provided is an antibody as described herein, which is a full length IgG1 antibody with mutations L234A, L235A and P329G (numbering according to the
25 EU index of Kabat).

In a particular embodiment, provided is an antibody as described herein, which is a full length IgG1 antibody with mutations L234A, L235A and P329G (numbering according to the EU index of Kabat).

In a further embodiment, provided is an antibody as described herein, which is cross
30 reactive for human and cynomolgus CD19.

The disclosure provides an antibody that is bispecific, wherein said antibody specifically binds to human CD19 and a second antigen binding moiety, wherein the antibody comprises

- (a) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 43,
- (b) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 44,
- 5 (c) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 45,
- (d) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 46,
- (e) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 47, and
- (f) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 48.

10 In another aspect, there is provided an antibody that is bispecific, wherein the antibody specifically binds to human CD19 and a second antigen, wherein the antibody comprises a VH domain comprising an amino acid sequence of SEQ ID NO:99 and a VL domain comprising an amino acid sequence of SEQ ID NO:100

According to the disclosure, there is provided an isolated polynucleotide encoding an antibody as defined herein before. According to another aspect, there is provided a
15 polynucleotide encoding the antibody as defined herein before. The disclosure further provides a vector, particularly an expression vector, comprising the isolated polynucleotide of the disclosure and a host cell comprising the isolated polynucleotide or the vector of the disclosure. According to another aspect, there is provided a vector, particularly an expression vector, comprising the polynucleotide as defined herein before. According to another aspect, there is provided a host
20 cell comprising the polynucleotide as defined herein before or the vector as defined herein before. In some embodiments the host cell is a eukaryotic cell, particularly a mammalian cell.

There is also provided a method for producing the antibody of the disclosure, comprising the steps of (i) culturing the host cell of the disclosure under conditions suitable for expression of the antigen binding molecule, and (ii) recovering the antigen binding molecule. In another aspect,
25 provided is a method of producing the antibody as defined herein before, comprising the steps of (i) culturing the host cell as defined herein under conditions suitable for expression of the antibody, and (ii) recovering the antibody. The disclosure also encompasses an antibody produced by the method of the disclosure.

The disclosure further provides a pharmaceutical composition comprising the antibody of
30 the disclosure and at least one pharmaceutically acceptable excipient. In another aspect, provided is a pharmaceutical formulation comprising the antibody as defined herein and a pharmaceutically acceptable carrier.

Also encompassed by the disclosure is the antibody of the disclosure, or the pharmaceutical composition of the disclosure, for use as a medicament. In another aspect, provided is the antibody as defined herein before for use as a medicament. There is provided the antibody of the disclosure, or the pharmaceutical composition of the disclosure, for use in the treatment of a disease in an individual in need thereof. There is provided the antibody of the disclosure, or the pharmaceutical composition of the disclosure, for use in the treatment of cancer. In another aspect, provided is the antibody as defined herein before for use in treating a B-cell cancer. In another aspect, provided is the antibody as defined herein before for use in depleting B-cells. There is provided the antibody of the disclosure, or the pharmaceutical composition of the disclosure, for use in the treatment autoimmune diseases, rheumatoid arthritis, lupus, psoriasis, or a bone disease. In another aspect, provided is the antibody as defined herein before for use in the treatment of autoimmune diseases, rheumatoid arthritis, lupus, psoriasis, or a bone disease.

Also provided is the use of the antibody of the disclosure for the manufacture of a medicament for the treatment of a disease in an individual in need thereof, in particular for the manufacture of a medicament for the treatment of cancer, as well as a method of treating a disease in an individual, comprising administering to said individual a therapeutically effective amount of a composition comprising the antibody in a pharmaceutically acceptable form. In another aspect, provided is use of the antibody as defined herein before in the manufacture of a medicament for the treatment of B cell cancer, autoimmune diseases, rheumatoid arthritis, lupus, or psoriasis. In an

Claims

1. An antibody that specifically binds to human CD19, wherein the antibody comprises a VH domain comprising an amino acid sequence of SEQ ID NO:99 and a VL domain comprising an amino acid sequence of SEQ ID NO:100.

5 2. The antibody according to claim 1, wherein the antibody is an antibody fragment that specifically binds to human CD19.

3. The antibody according to claim 1, which is a full length IgG1 antibody.

4. The antibody of according to claims 1 or 3, which is a full length IgG1 antibody with mutations L234A, L235A and P329G (numbering according to the EU index of Kabat).

10 5. The antibody according to any one of claims 1 to 4, wherein the antibody is cross reactive for human and cynomolgus CD19.

15 6. An antibody that is bispecific, wherein said antibody specifically binds to human CD19 and a second antigen, wherein the antibody comprises a VH domain comprising an amino acid sequence of SEQ ID NO:99 and a VL domain comprising an amino acid sequence of SEQ ID NO:100.

7. A polynucleotide encoding the antibody according to any one of claims 1 to 6.

8. A vector, particularly an expression vector, comprising the polynucleotide according to claim 7.

9. A host cell comprising the polynucleotide of claim 7 or the vector of claim 8.

20 10. A method of producing the antibody according to claims 1 to 6, comprising the steps of (i) culturing the host cell according to claim 9 under conditions suitable for expression of the antibody, and (ii) recovering the antibody.

11. A pharmaceutical formulation comprising the antibody according to any one of claims 1 to 6 and a pharmaceutically acceptable carrier.

25 12. The antibody according to any one of claims 1 to 6 for use as a medicament.

13. The antibody according to any one of claims 1 to 6 for use in treating a B-cell cancer.

14. The antibody according to any one of claims 1 to 6 for use in depleting B-cells.

15. The antibody according to any one of claims 1 to 6 for use in the treatment of autoimmune diseases, rheumatoid arthritis, lupus, or psoriasis.

16. Use of the antibody according to any one of claims 1 to 6 in the manufacture of a
5 medicament for the treatment of B cell cancer, autoimmune diseases, rheumatoid arthritis, lupus, or psoriasis.
