

CLAIMS

1. A pharmaceutical combination comprising:

(A) an anti-LY75 antibody, or an antigen-binding portion thereof, which competes for binding to LY75 with an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2;

or

an anti-LY75 antibody, or an antigen-binding portion thereof, said antibody or portion thereof comprising:

a) a heavy chain variable region comprising:

- i) a first vhCDR comprising SEQ ID NO: 5;
- ii) a second vhCDR comprising SEQ ID NO: 6; and
- iii) a third vhCDR comprising SEQ ID NO: 7; and

b) a light chain variable region comprising:

- i) a first vlCDR comprising SEQ ID NO: 8;
- ii) a second vlCDR comprising SEQ ID NO: 9; and
- iii) a third vlCDR comprising SEQ ID NO: 10;

optionally wherein any one or more of the above SEQ ID NOs independently comprise one, two, three, four or five amino acid substitutions, additions or deletions;

and

(B) an anti-CD20 antibody, or an antigen-binding portion thereof, said antibody or portion thereof comprising:

a) a heavy chain variable region comprising:

- i) a first vhCDR comprising SEQ ID NO: 40;
- ii) a second vhCDR comprising SEQ ID NO: 41; and
- iii) a third vhCDR comprising SEQ ID NO: 42; and

b) a light chain variable region comprising:

- i) a first vlCDR comprising SEQ ID NO: 43;
- ii) a second vlCDR comprising SEQ ID NO: 44; and
- iii) a third vlCDR comprising SEQ ID NO: 45;

optionally wherein any one or more of the above SEQ ID NOs independently comprise one, two, three, four or five amino acid substitutions, additions or deletions;

5 wherein the pharmaceutical combination is in the form of a combined preparation for simultaneous, separate or sequential use, preferably for the treatment of cancer.

2. A pharmaceutical combination comprising:

10 (A) an anti-LY75 antibody, or an antigen-binding portion thereof, which competes for binding to LY75 with an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2;

15 or

an anti-LY75 antibody, or an antigen-binding portion thereof, said antibody or portion thereof comprising:

a) a heavy chain variable region comprising:

- 20 i) a first vhCDR comprising SEQ ID NO: 5;
ii) a second vhCDR comprising SEQ ID NO: 6; and
iii) a third vhCDR comprising SEQ ID NO: 7; and

b) a light chain variable region comprising:

- 25 i) a first vlCDR comprising SEQ ID NO: 8;
ii) a second vlCDR comprising SEQ ID NO: 9; and
iii) a third vlCDR comprising SEQ ID NO: 10;

optionally wherein any one or more of the above SEQ ID NOs independently comprise one, two, three, four or five amino acid substitutions, additions or deletions;

and

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(B) ibrutinib or a pharmaceutically-acceptable salt thereof,

wherein the pharmaceutical combination is in the form of a combined preparation for simultaneous, separate or sequential use, preferably for the treatment of cancer.

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3. A pharmaceutical combination as claimed in claim 1 or claim 2, wherein any one or more of SEQ ID NOs: 5-10 independently comprise one, two, three, four or five conservative amino acid substitutions.

4. A pharmaceutical combination as claimed in claim 3, wherein any one or more of SEQ ID NOs: 5-10 independently comprise one or two conservative amino acid substitutions.

5. The pharmaceutical combination as claimed in any one of claims 1 to 4, wherein the anti-LY75 antibody or an antigen-binding portion thereof comprises a heavy chain variable region having at least 80%, 85%, 90%, 95%, 99% or 100% amino acid sequence identity to SEQ ID NO: 1 and a light chain variable region having at least 80%, 85%, 90%, 95%, 99% or 100% amino acid sequence identity to SEQ ID NO: 2.

6. The pharmaceutical combination as claimed in any one of claims 1 to 5, wherein the anti-LY75 antibody is a human IgG1 monoclonal antibody.

7. The pharmaceutical combination according to any one of claims 1 to 6, wherein the anti-LY75 antibody or an antigen-binding portion thereof further comprises a covalently-attached moiety.

8. The pharmaceutical combination according to claim 7, wherein said moiety is a drug.

9. The pharmaceutical combination according to claim 8, wherein said drug is a maytansinoid or a derivative thereof.

10. The pharmaceutical combination according to claim 9, wherein said drug is DM4 or DM1.

11. A pharmaceutical combination as claimed in any one of claims 1 or 3 to 10, wherein any one or more of SEQ ID NOs: 40-45 independently comprise one, two, three, four or five conservative amino acid substitutions.

12. A pharmaceutical combination as claimed in claim 11, wherein any one or more of SEQ ID NOs: 40-45 independently comprise one or two conservative amino acid substitutions.

13. The pharmaceutical combination according to any one of claims 1 or 3 to 12, wherein the anti-CD20 antibody is a mouse/human chimeric antibody, a humanised antibody or a human antibody.

5 14. The pharmaceutical combination according to any one of claims 1 or 3 to 13, wherein the anti-CD20 antibody is Rituximab.

15. The pharmaceutical combination according to any one of claims 1 to 14, wherein (A) and/or (B) additionally comprise one or more pharmaceutically-acceptable diluents, excipients or
10 carriers.

16. The pharmaceutical combination according to any one of claims 1 to 15, wherein the pharmaceutical combination is in the form of a combined preparation for simultaneous, separate or sequential use for the treatment of diffuse large B-cell lymphoma (DLBCL) or Non-Hodgkin's
15 lymphoma.

17. The pharmaceutical combination according to any one of claims 1 to 16, further comprising instructions for treating cancer in a patient in need of such treatment by administering (A) and (B) to the patient.
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18. A kit comprising:
(i) an expression vector comprising DNA encoding the heavy and light chains of the anti-LY75 antibody or antigen-binding portion thereof of claim 1; and
(ii) an expression vector comprising DNA encoding the heavy and light chains of the anti-
25 CD20 antibody or antigen-binding portion thereof of claim 1.

19. A host cell comprising expression vectors comprising nucleic acids encoding:
(i) the heavy chain of the anti-LY75 antibody or antigen-binding portion thereof of claim 1;
(ii) the light chain of the anti-LY75 antibody or antigen-binding portion thereof of claim 1;
30 (iii) the heavy chain of the anti-CD20 antibody or antigen-binding portion thereof of claim 1; and
(iv) the light chain of the anti-CD20 antibody or antigen-binding portion thereof of claim 1.

20. A pharmaceutical combination according to any one of claims 1 to 15, for use in the treatment of cancer, wherein components (A) and (B) are simultaneously, separately or
35 sequentially administered to the patient for the treatment of the cancer.

21. The pharmaceutical combination for use according to claim 20, wherein the anti-LY75 antibody or antigen-binding portion thereof is internalized by a cell expressing LY75.
22. The pharmaceutical combination for use according to claim 20 or 21, wherein the anti-LY75 antibody or antigen-binding portion comprises a covalently-attached drug conjugate.
23. The pharmaceutical combination for use according to claim 22, wherein the covalently-attached drug conjugate is a maytansinoid, preferably DM4.
24. The pharmaceutical combination for use according to any one of claims 20 to 23, wherein the cancer is diffuse large B-cell lymphoma (DLBCL) or Non-Hodgkin's lymphoma.
25. Use of components (A) and (B) of the pharmaceutical combination as defined in any one of claims 1 to 15 in the manufacture of a pharmaceutical combination for simultaneous, separate or sequential use for the treatment of cancer.
26. The use according to claim 25, wherein the anti-LY75 antibody or antigen-binding portion thereof is internalized by a cell expressing LY75.
27. The use according to claim 25 or 26, wherein the anti-LY75 antibody or antigen-binding portion comprises a covalently-attached drug conjugate.
28. The use according to claim 27, wherein the covalently-attached drug conjugate is a maytansinoid, preferably DM4.
29. The use according to any one of claims 25 to 28, wherein the cancer is diffuse large B-cell lymphoma (DLBCL) or Non-Hodgkin's lymphoma.
30. A pharmaceutical combination according to any one of claims 1 to 16 for use in therapy or for use as a medicament.