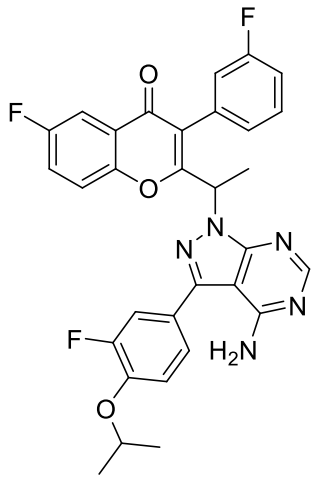
CLAIMS

1. An *in vitro* method of inhibiting proliferation of a cell population comprising contacting the population with a combination comprising

(i) a compound of formula A,



(A)

a stereoisomer thereof, or a pharmaceutically acceptable salt, or solvate thereof, and

(ii) an anti-CD20 antibody or antigen-binding fragment thereof.

2. The method of claim 1, wherein said anti-CD20 antibody is ublituximab or binds to the same epitope as ublituximab or is an antigen-binding fragment of said antibody.

3. The method of claim 1, wherein said antibody or fragment comprises the VH CDR1, CDR2 and CDR3 region of sequences SEQ ID NO: 1, 2, and 3, and the VL CDR1, CDR2 and CDR3 region of sequences SEQ ID NO: 6, 7, and 8, optionally, wherein the anti-CD20 antibody or antigen-binding fragment thereof comprises the VH of SEQ ID NO: 4 and the VL of SEQ ID NO: 9.

4. The method of any one of claims 1-3 wherein said compound of formula A is (RS)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-

(3-fluorophenyl)-4H-chromen-4-one; (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one; or (R)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one.

5. The method of any one of claims 1-4, wherein the population is contacted with a composition comprising

(i) a compound selected from the group consisting of (RS)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one; (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one; and (R)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one, and

(ii) the anti-CD20 antibody.

6. The method of any one of claims 1-5, wherein the population is contacted with

(i) a first composition comprising a compound selected from the group consisting of (RS)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one; (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one; and (R)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one, and

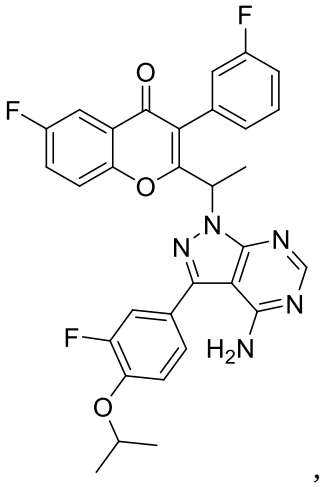
(ii) a second composition comprising the anti-CD20 antibody.

7. The method of any one of claims 1-6, wherein the anti-CD20 antibody is ublituximab.

8. The method of any one of claims 1-7, wherein the compound of formula A is (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one.

9. A therapeutic combination comprising:

(i) a compound of formula A,



(A)

a stereoisomer thereof, or a pharmaceutically acceptable salt, or solvate thereof;
and
(ii) an anti-CD20 antibody or antigen-binding fragment thereof,
for use as a medicament for treating a disease or disorder associated with excessive B-cell proliferation, cancer or an autoimmune disease or disorder.

10. A compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, for use as a medicament in a method for treating a disease or disorder associated with excessive B-cell proliferation, cancer or an autoimmune disease or disorder, the method comprising administering the compound in combination with an anti-CD20 antibody or antigen binding fragment thereof.

11. An anti-CD20 antibody or antigen binding fragment thereof for use as a medicament in a method for treating a disease or disorder associated with excessive B-cell proliferation, cancer or an autoimmune disease or disorder, the method comprising administering the anti-CD20 antibody or fragment in combination with a compound of formula (A) or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof.

12. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or antigen-

binding fragment thereof, for use according to any one of claims 9-11, wherein said anti-CD20 antibody is ublituximab or binds to the same epitope as ublituximab, or is an antigen-binding fragment of said antibody.

13. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or an antigen-binding fragment thereof, for use according to any one of claims 9-11, wherein said anti-CD20 antibody is selected from the group consisting of rituximab, ofatumumab, ocrelizumab, veltuzumab, GA101, AME-133v, PRO131921, tositumomab, hA20, and PRO70769, or is an antigen-binding fragment of said antibody.

14. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or an antigen-binding fragment thereof, for use according to any one of claims 9-13 wherein the compound is selected from (RS)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one; (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one; and (R)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one.

15. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or an antigen-binding fragment thereof, for use according to any one of claims 9-12 or 14, wherein the anti-CD20 antibody is ublituximab.

16. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or an antigen-binding fragment thereof, for use according to any one of claims 9-15, wherein the compound of formula A is (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one.

17. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or an antigen-binding fragment thereof, for use according to any one of claims 9-12 and 14-16 wherein said compound is a p-toluenesulfonate salt of (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one, and said anti-CD20 antibody is ublituximab.

18. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or an antigen-binding fragment thereof, use according to any one of claims 9-17, wherein the cancer is a hematological malignancy, optionally wherein the hematological malignancy is lymphoma or leukemia, optionally wherein the hematological malignancy is selected from the group consisting of acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), multiple myeloma (MM), non-Hodgkin's lymphoma (NHL), mantle cell lymphoma (MCL), follicular lymphoma, Waldenstrom's macroglobulinemia (WM), B-cell lymphoma and diffuse large B-cell lymphoma (DLBCL).

19. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or antigen-binding fragment thereof, for use according to any one of claims 9-18, wherein the cancer overexpresses CD20 and/or wherein the cancer is refractory to chemotherapy.

20. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or antigen-binding fragment thereof, for use according to any one of claims 9-19, wherein the subject has previously been treated with chemotherapy, rituximab, or a combination thereof.

21. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or antigen-binding fragment thereof, for use according to any one of claims 9-20, wherein said compound and said anti-CD20 antibody or fragment are administered to the subject sequentially or

simultaneously, optionally wherein said compound of formula A and said anti-CD20 antibody or fragment are contained in the same pharmaceutical composition or separate pharmaceutical compositions.

22. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or antigen-binding fragment thereof, for use according to any one of claims 9-21, wherein said method comprises administering or said therapeutic combination comprises at least one additional therapeutic agent, optionally wherein the additional therapeutic agent is selected from the group consisting of a proteasome inhibitor, Bortezomib (Velcade®), Carfilzomib (PR-171), PR-047, disulfiram, lactacystin, PS-519, eponemycin, epoxomycin, aclacinomycin, CEP-1612, MG-132, CVT-63417, PS-341, vinyl sulfone tripeptide inhibitors, ritonavir, PI-083, (+/-)-7-methylomuralide, (-)-7-methylomuralide, lenalidomide, and combinations thereof.

23. The therapeutic combination, the compound of formula (A), or a stereoisomer thereof, a pharmaceutically acceptable salt, or solvate thereof, or the anti-CD20 antibody or antigen-binding fragment thereof, for use according to any one of claims 9-22, wherein said method comprises administering or said therapeutic combination comprises at least two additional therapeutic agents selected from the group consisting of:

a) CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone);

b) R-CHOP (rituximab-CHOP);

c) hyperCV AD (hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone, methotrexate, cytarabine);

d) R-hyperCV AD (rituximab-hyperCV AD);

e) FCM (fludarabine, cyclophosphamide, mitoxantrone);

f) R-FCM (rituximab, fludarabine, cyclophosphamide, mitoxantrone);

g) bortezomib and rituximab;

h) temsirolimus and rituximab;

i) temsirolimus and Velcade.RTM.;

j) Iodine-131 tositumomab (Bexxar.RTM.) and CHOP;

k) CVP (cyclophosphamide, vincristine, prednisone);

l) R-CVP (rituximab-CVP);

m) ICE (iphosphamide, carboplatin, etoposide);

n) R-ICE (rituximab-ICE);

o) FCR (fludarabine, cyclophosphamide, rituximab);

p) FR (fludarabine, rituximab); and

q) D.T. PACE (Dexamethasone, Thalidomide, Cisplatin, Adriamycin, Cyclophosphamide, Etoposide).

24. A kit comprising (i) a compound of formula A, a stereoisomer thereof, or a pharmaceutically acceptable salt, or solvate thereof, and (ii) an anti-CD20 antibody or antigen-binding fragment thereof.

25. A kit according to claim 24, wherein said anti-CD20 antibody is ublituximab or binds to the same epitope as ublituximab, or is an antigen-binding fragment of said antibody.

26. A kit according to claim 24, wherein said anti-CD20 antibody is selected from the group consisting of rituximab, ofatumumab, ocrelizumab, veltuzumab, GA101, AME-133v, PRO131921, tositumomab, hA20, and PRO70769, or is an antigen-binding fragment of said antibody.

27. A kit according to any of claims 24-26, wherein the compound of formula A is selected from the group consisting of (RS)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one; (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one; and (R)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one.

28. The kit of any one of claims 24, 25 or 27, wherein said anti-CD20 antibody is ublituximab.

29. The kit of any one of claims 24-28, wherein said compound of formula A is (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one.

30. The kit of any one of claims 24, 25 or 27-29, wherein said compound is a p-toluenesulfonate salt of (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one, and said anti-CD20 antibody is ublituximab.

31. The kit of any one of claims 24-30, wherein said anti-CD20 antibody or fragment and said compound are contained within the same composition or are in separate compositions.

32. The kit of any one of claims 24-31, further comprising one or more additional active agents.

33. A pharmaceutical composition comprising

(i) a compound of formula A selected from the group consisting of (RS)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one; (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one; and (R)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one, and

(ii) an anti-CD20 antibody or an antigen-binding fragment thereof.

34. The pharmaceutical composition of claim 33, wherein said anti-CD20 antibody is ublituximab or binds the same epitope as ublituximab or is an antigen-binding fragment of said antibody.

35. The pharmaceutical composition of claim 33 or 34, wherein said compound of formula A is (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one.

36. The pharmaceutical composition according to any one of claims 33-35, wherein said compound is a p-toluenesulfonate salt of (S)-2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-fluoro-3-(3-fluorophenyI)-4H-chromen-4-one, and said anti-CD20 antibody is ublituximab.