

CLAIMS

1. Use of an immunoconjugate that binds to CD37 comprising (i) an antibody or antigen-binding fragment thereof comprising VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 sequences as set forth in SEQ ID NOs: 4-9, respectively and (ii) a maytansinoid; and

an anti-CD20 antibody or antigen-binding fragment thereof in the manufacture of a medicament for the treatment of B-cell cancer in a patient.
2. The use of claim 1, wherein the immunoconjugate that binds to CD37 comprises an antibody or antigen-binding fragment thereof that competitively inhibits the binding of an antibody with the sequences of SEQ ID NOs: 12 and 15 to CD37.
3. The use of claim 1, wherein the immunoconjugate that binds to CD37 comprises an antibody or antigen-binding fragment thereof the variable heavy chain sequence set forth in SEQ ID NO: 12 and the variable light chain sequence set forth in SEQ ID NO: 15.
4. The use of claim 3, wherein the immunoconjugate that binds to CD37 comprises an antibody comprising the full-length heavy chain amino acid sequence set forth in SEQ ID NO: 18 and the full-length light chain amino acid sequence set forth in SEQ ID NO: 21.
5. The use of any of claims 1-4, wherein the maytansinoid is DM1.
6. The use of any one of claims 1-5, wherein the immunoconjugate that binds to CD37 comprises a non-cleavable linker.
7. The use of claim 6, wherein the linker is SMCC.
8. The use of any one of claims 1-7, wherein the immunoconjugate that binds to CD37 comprises an antibody comprising the full-length heavy chain amino acid sequence set forth in SEQ ID NO: 18 and the full-length light chain amino acid sequence set forth in SEQ ID NO: 21 linked to DM1 by an SMCC linker.
9. The use of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is selected from the group consisting of rituximab, ofatumumab, obinutuzumab, and veltuzumab.
10. The use of claim 9, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is veltuzumab.
11. The use of claim 9, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is selected from the group consisting of rituximab, ofatumumab, and obinutuzumab.

12. The use of claim 11, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is rituximab.
13. The use of claim 11, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is ofatumumab.
14. The use of claim 11, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is obinutuzumab.
15. The use of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is a type I antibody or antigen-binding fragment thereof.
16. The use of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is not rituximab.
17. The use of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is not ofatumumab.
18. The use of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is a type II antibody or antigen binding fragment thereof.
19. The use of any one of claims 1-18, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 produce a synergistic effect.
20. The use of any one of claims 1-18, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 produce a Synergy Score of at least 4 *in vitro*.
21. The use of claim 20, wherein the Synergy Score is at least 10.
22. The use of claim 21, wherein the Synergy Score is at least 20.
23. The use of claim 22, wherein the Synergy Score is at least 30.
24. The use of claim 23, wherein the Synergy Score is at least 40.
25. The use of any one of claims 1-24, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 have a combination index value of less than 0.5.
26. The use of any one of claims 1-25, wherein administration of the immunoconjugate that binds CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 does not produce more toxicity than administration of the immunoconjugate that binds CD37 alone.

27. The use of any one of claims 1-26, wherein administration of the immunoconjugate that binds CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 does not produce more toxicity than administration of the antibody that binds to CD20 alone.
28. The use of any one of claims 1-27, wherein administration of the immunoconjugate that binds CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 does not produce more toxicity than administration of R-CHOP.
29. The use of claim 28, wherein administration of the immunoconjugate that binds CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 produces less toxicity than administration of R-CHOP.
30. The use of any one of claims 1-29, wherein the cancer is leukemia or lymphoma.
31. The use of any one of claims 1-30, wherein the cancer is selected from the group consisting of B-cell lymphomas including NHL, precursor B-cell lymphoblastic leukemia/lymphoma and mature B-cell neoplasms, such as B-cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, mantle cell lymphoma (MCL), follicular lymphoma (FL), including low-grade, intermediate-grade and high-grade FL, cutaneous follicle center lymphoma, marginal zone B-cell lymphoma (MALT type, nodal and splenic type), hairy cell leukemia, diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma, plasmacytoma, plasma cell myeloma, post-transplant lymphoproliferative disorder, Waldenstrom's macroglobulinemia, acute lymphoblastic leukemia (ALL), and anaplastic large-cell lymphoma (ALCL).
32. The use of claim 31, wherein the cancer is NHL.
33. The use of claim 32, wherein the NHL is relapsed or refractory NHL.
34. The use of claim 32 or 33, wherein the NHL is diffuse large B-cell lymphoma (DLBCL).
35. The use of claim 34, wherein the DLBCL is GCB DLBCL.
36. The use of claim 34, wherein the DLBCL is ABC DLBCL.
37. The use of claim 32 or 33, wherein the NHL is mantle cell lymphoma (MCL).
38. The use of claim 32 or 33, wherein the NHL is chronic lymphocytic leukemia (CLL).
39. The use of claim 32 or 33, wherein the NHL is follicular lymphoma.
40. The use of any one of claims 1-39, wherein the cancer overexpresses MYC.
41. The use of any one of claims 1-40, wherein the cancer overexpresses BCL2.

42. The use of claim 40 or 41, wherein the cancer overexpresses MYC and BCL2.
43. The use of any one of claims 1-42, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 are to be administered simultaneously.
44. The use of claim 43, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 are to be administered in separate pharmaceutical compositions.
45. The use of claim 43, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 are to be administered in the same pharmaceutical composition.
46. The use of any one of claims 1-42, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 are to be administered sequentially.
47. The use of any one of claims 1-46, wherein the immunoconjugate is to be administered at a dose of from 0.1 mg/kg to 2.8 mg/kg.
48. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of from 0.4 mg/kg to 2.8 mg/kg.
49. The use of claim 48, wherein the immunoconjugate is to be administered at a dose of from 0.4 mg/kg to 2.0 mg/kg.
50. The use of claim 49, wherein the immunoconjugate is to be administered at a dose of from 0.4 mg/kg to 1.4 mg/kg.
51. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of from 0.7 mg/kg to 1.8 mg/kg.
52. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of from 1.4 mg/kg to 2.8 mg/kg.
53. The use of claim 52, wherein the immunoconjugate is to be administered at a dose of from 1.4 mg/kg to 2.0 mg/kg.
54. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of from 2.0 mg/kg to 2.8 mg/kg.
55. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 0.7 mg/kg.

56. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 1.0 mg/kg.
57. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 1.4 mg/kg.
58. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 1.6 mg/kg.
59. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 1.8 mg/kg.
60. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 2.0 mg/kg.
61. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 2.2 mg/kg.
62. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 2.4 mg/kg.
63. The use of claim 47, wherein the immunoconjugate is to be administered at a dose of 2.8 mg/kg.
64. The use of any one of claims 1-46, wherein the immunoconjugate is to be administered at a dose of 3.0 mg/kg.
65. The use of any one of claims 1-64, wherein the immunoconjugate is to be administered once every three weeks.
66. The use of claim 65, wherein the immunoconjugate is to be administered on day 1 of a 21-day cycle.
67. The use of any one of claims 1-66, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is to be administered at a dose of 375 mg/m².
68. The use of any one of claims 1-67, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is to be administered once every week.
69. The use of any one of claims 1-67, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is to be administered on week 1, day 1 of a three week schedule.
70. The use of any one of claims 1-66, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is to be administered at a dose of 500 mg/m².

71. The use of any one of claims 1-64 and 66, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is to be administered once every 28 days.
72. The use of any one of claims 1-67, wherein the immunoconjugate that binds to CD37 and the antibody or antigen-binding fragment thereof that binds to CD20 are to be administered intravenously.
73. The use of any one of claims 1-72, wherein the medicament is for use with a corticosteroid.
74. The use of claim 73, wherein the corticosteroid is to be administered prior to the administration of the immunoconjugate.
75. The use of claim 74, wherein the corticosteroid is to be administered from 30 to 60 minutes prior to administration of the immunoconjugate.
76. The use of claim 73, wherein the corticosteroid is to be administered peri-infusionally.
77. The use of claim 73, wherein the corticosteroid is to be administered during the administration of the immunoconjugate.
78. The use of any one of claims 74, 75, or 77, wherein the corticosteroid is to be administered at least one additional time from one day to four days after the administration of the immunoconjugate.
79. The use of any one of claims 74, 75, or 77, wherein the corticosteroid is to be administered at least one additional time from one day to three days after the administration of the immunoconjugate.
80. The use of any one of claims 74, 75, or 77, wherein the corticosteroid is to be administered at least two additional times.
81. The use of claim 74, 75, or 77, wherein the corticosteroid is to be further administered on day two and day three after the administration of the immunoconjugate.
82. The use of claim 73, wherein the corticosteroid is to be administered after the administration of the immunoconjugate.
83. The use of any one of claims 73-82, wherein the corticosteroid is selected from the group consisting of prednisone, prednisolone, methylprednisolone, beclamethasone, betamethasone, dexamethasone, fludrocortisone, hydrocortisone, and triamcinolone.
84. The use of claim 82, wherein the corticosteroid is dexamethasone.
85. The use of any one of claims 1-84, wherein the medicament is for use with a growth factor.

86. The use of claim 85, wherein the growth factor is selected from the group consisting of granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), macrophage colony-stimulating factor (M-CSF), filgrastim, and pegfilgrastim.
87. The use of claim 86, wherein the growth factor is G-CSF.
88. The use of any one of claims 84-86, wherein the growth factor is to be administered early to mid-cycle.
89. The use of any one of claims 84-86, wherein the growth factor is to be administered at least once from day one to day twelve after the administration of the immunoconjugate.
90. The use of any one of claims 1-89, wherein the cancer expresses CD37.
91. The use of any one of claims 1-89, wherein the cancer expresses CD20.
92. The use of any one of claims 1-89, wherein the cancer expresses CD37 and CD20.
93. The use of claim 1, wherein the immunoconjugate is IMG529, wherein the immunoconjugate is to be administered at a dose of 0.7 mg/kg once every three weeks, wherein the antibody or antigen-binding fragment thereof that binds to CD20 is rituximab, and wherein the antibody or antigen-binding fragment thereof that binds to CD20 is to be administered at a dose of 375 mg/m² on week 1, day 1 of a three week schedule.
94. An immunoconjugate that binds to CD37 comprising (i) an antibody or an antigen-binding fragment thereof comprising VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 sequences as set forth in SEQ ID NOs: 4-9, respectively and (ii) a maytansinoid; and

an anti-CD20 antibody or antigen-binding fragment thereof for use in the treatment of B-cell cancer in a patient.