

CLAIMS

1. A method of selecting an individual as suitable for treatment with an anti-CD25 ADC, wherein the individual is selected for treatment with the anti-CD25 ADC if the individual has been treated with an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent.
2. A method of selecting an individual as suitable for treatment with an anti-CD25 ADC, wherein the individual is selected for treatment with the anti-CD25 ADC if the individual is being treated with an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent.
3. The method according to any one of the preceding claims, wherein the individual is selected for treatment if the individual is refractory to treatment, or further treatment, with the anti-BCL-2 agent, mTOR inhibitor, or secondary agent.
4. A method for treating a disorder in an individual, the method comprising:
 - (i) selecting an individual as suitable for treatment by a method according to any one of claims 1 to 3; and
 - (ii) administering to the individual an effective amount of the anti-CD25 ADC.
5. The method according to claim 4, further comprising administering a an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent in combination with the anti-CD25 ADC.
6. A method for treating a disorder in an individual, the method comprising administering to the individual an effective amount of an anti-CD25 ADC and an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent.
7. The method according to claim 6, wherein the individual is selected for treatment according to a method according to any one of claims 1 to 3.
8. The method according to any one of claims 5 to 7, wherein the treatment comprises administering the anti-CD25 ADC before the anti-BCL-2 agent, mTOR inhibitor, or secondary agent secondary agent, simultaneous with the anti-BCL-2 agent, mTOR inhibitor, or secondary agent, or after the anti-BCL-2 agent, mTOR inhibitor, or secondary agent.
9. The method according to any previous claim, wherein the treatment further comprises administering a chemotherapeutic agent.
10. The method according to any previous claim, wherein the individual is human.
11. The method according to any preceding claim, wherein the individual has a disorder or has been determined to have a disorder.

12. The method according to claim 11, wherein the individual has, or has been has been determined to have, a cancer which expresses CD25 or CD25+ tumour-associated non-tumour cells, such as CD25+ infiltrating cells.
13. The method according to any previous claim, wherein the individual is undergoing treatment with an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent.
14. The method according to any previous claim, wherein the individual has undergone treatment with an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent.
15. The method according to any previous claim, wherein the individual is refractory to treatment, or further treatment, with the anti-BCL-2 agent, mTOR inhibitor, or secondary agent.
16. The method according to any one of the preceding claims, wherein the treatment has increased efficacy as compared to monotherapy with either the anti-CD25 ADC or anti-BCL-2 agent, mTOR inhibitor, or secondary agent alone.
17. The method according to any preceding claim, wherein the anti-CD25 ADC is ADCx25 or ADCT-301.
18. The method according to any previous claim, wherein the disorder is a proliferative disease.
19. The method of claim 18, wherein the disorder is cancer.
20. The method according to any previous claim, wherein the individual has, or has been has been determined to have, a disorder characterised by the presence of a neoplasm comprising both CD25+ve and CD25-ve cells.
21. The method according to any previous claim, wherein the individual has, or has been has been determined to have, a disorder characterised by the presence of a neoplasm comprising, or composed of, CD25-ve neoplastic cells.
22. The method according to either of claims 20 or 21, wherein the neoplasm is all or part of a solid tumour.
23. The method of statement 22, wherein the solid tumour is associated with CD25+ve infiltrating cells;
optionally wherein the solid tumour is associated with high levels of CD25+ve infiltrating cells.
24. The method of statement 23, wherein the solid tumour is selected from the group consisting of pancreatic cancer, breast cancer (including triple negative breast cancer), colorectal cancer, gastric and oesophageal cancer, melanoma, non-small cell lung

cancer, ovarian cancer, hepatocellular carcinoma, renal cell carcinoma, bladder, and head and neck cancer.

25. The method according to any previous claim, wherein the disorder is selected from the group comprising:

Hodgkin's and non-Hodgkin's Lymphoma, including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, (FL), Mantle Cell lymphoma (MCL), chronic lymphatic lymphoma (CLL), Marginal Zone B-cell lymphoma (MZBL);

leukemias such as Hairy cell leukemia (HCL), Hairy cell leukemia variant (HCL-v), Acute Myeloid Leukaemia (AML), anaplastic large cell lymphoma (ALCL), and Acute Lymphoblastic Leukaemia (ALL) such as Philadelphia chromosome-positive ALL (Ph+ALL) or Philadelphia chromosome-negative ALL (Ph-ALL);

pancreatic cancer, breast cancer, colorectal cancer, gastric and oesophageal cancer, leukemia and lymphoma, melanoma, non-small cell lung cancer, ovarian cancer, hepatocellular carcinoma, renal cell carcinoma, and head and neck cancer.

26. The method according to any one of claims 1 to 25, wherein the secondary agent is bendamustine.

27. The method according to any one of claims 1 to 25, wherein the secondary agent is a phosphoinositide 3-kinase inhibitor.

28. The method according to claim 27, wherein the phosphoinositide 3-kinase inhibitor is copanlisib, idelalisib, duvelisib, Taselisib, Buparlisib, Alpelisib, Umbralisib, Dactolisib, or Voxtalisisib.

29. The method according to claim 27, wherein the phosphoinositide 3-kinase inhibitor is copanlisib or idelalisib.

30. The method according to any one of claims 1 to 25, wherein the secondary agent is a proteasome inhibitor.

31. The method according to claim 30, wherein the proteasome inhibitor is bortezomib, carfilzomib, Ixazomib, Oprozomib, or Salinosporamide A.

32. The method according to claim 30, wherein the wherein the proteasome inhibitor is bortezomib.

33. The method according to any one of claims 1 to 25, wherein the secondary agent is an anti-folate.

34. The method according to claim 33, wherein the anti-folate is pralatrexate, methotrexate, pemetrexed, or raltitrexed.

35. The method according to claim 33, wherein the anti-folate is pralatrexate.

36. The method according to any one of claims 1 to 25, wherein the secondary agent is a HDAC inhibitor.
37. The method according to claim 36, wherein the HDAC inhibitor is romidepsin, vorinostat, Abexinostat, belinostat (PXD101), LAQ824, panobinostat (LBH589), entinostat (MS-275), tacedinaline (CI994), or mocetinostat (MGCD0103).
38. The method according to claim 36, wherein the HDAC inhibitor is romidepsin or vorinostat.
39. The method according to any one of claims 1 to 25, wherein the anti-BCL-2 agent is selected from the group consisting of: Venetoclax (ABT-199), navitoclax (ABT-263), ABT-737, S55746/BCL201, and oblimersen (G3139).
40. The method according to claim 39, wherein the anti-BCL-2 agent is Venetoclax.
41. The method according to any one of claims 1 to 25, wherein the mTOR inhibitor is everolimus (RAD001), sirolimus (Rapamycin), CCI-779 (temsirolimus), ridaforolimus (AP-23573), NVP-BEZ235 (dactolisib), BGT226, SF1126, Gedatolisib, Omipalisib, XL765, KU-0063794, oleuropein aglycone, AZD8055, AZD2014, AZD 3147, sapanisertib (INK128/MLN0128), OSI027, torin 1, torin 2, torkinib (PP242), WYE687, ETP45658, PF05212384, PF04691502, XL388, eCF309, RapaLink-1, or Rapalink-2.
42. The method according to claim 41, wherein the mTOR inhibitor is Everolimus.
43. An anti-CD25 ADC for use in a method of treatment according to any one of claims 4 to 42.
44. A composition comprising an anti-CD25 ADC, for use in a method of treatment according to any one of claims 4 to 42.
45. An anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent for use in a method of treatment according to any one of claims 5 to 42.
46. A composition comprising an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent for use in a method of treatment according to any one of claims 5 to 42.
47. Use of an anti-CD25 ADC in the manufacture of a medicament for treating a disorder in an individual, wherein the treatment comprises the method of any one of claims 4 to 42.
48. Use of an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent in the manufacture of a medicament for treating a disorder in an individual, wherein the treatment comprises the method of any one of claims 5 to 42.
49. A kit comprising:

a first medicament comprising an anti-CD25 ADC;
a package insert comprising instructions for administration of the first medicament according to the method of any one or claims 4 to 42.

50. The kit according to claim 49, further comprising:

A second medicament comprising an anti-BCL-2 agent, a mTOR inhibitor, or a secondary agent.