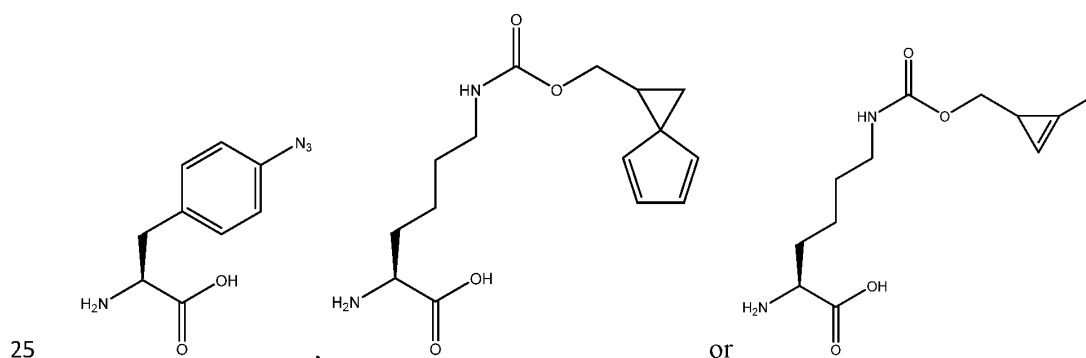


Claims

1. A dendrimer-targeting agent conjugate, comprising:
 - a) a dendrimer comprising
 - i) a core unit (C); and
 - ii) building units (BU), each building unit being a lysine residue or an analogue thereof;wherein the core unit is covalently attached to at least two building units *via* amide linkages, each amide linkage being formed between a nitrogen atom present in the core unit and a carbon atom of an acyl group present in a building unit;
 - b) a HER2 targeting agent which is a peptidic moiety having a molecular weight of up to about 80 kDa and comprising an antigen-binding site, which is covalently linked to the dendrimer by a spacer group;
 - c) a therapeutic agent which is covalently linked to a surface building unit of the dendrimer; and
 - d) a hydrophilic polymeric group that is covalently linked to surface building units of the dendrimer.
2. A conjugate as claimed in claim 1, wherein the peptidic moiety is selected from: a heavy chain antibody, Fab, Fv, scFv or a single domain antibody.
3. A conjugate as claimed in claim 1 or claim 2, wherein the peptidic moiety comprises or consists of a heavy chain variable (V_H) domain.
4. A conjugate as claimed in any of claims 1 to 3, wherein the peptidic moiety comprises or consists of a light chain variable (V_L) domain.
5. A conjugate as claimed in any of claims 1 to 4, wherein the targeting agent has a molecular weight of about 5 kDa to about 30 kDa.
6. A conjugate as claimed in claim 5, wherein the targeting agent has a molecular weight of about 5 kDa to about 15 kDa.

7. A conjugate as claimed in claim 6, wherein the targeting agent has a molecular weight of about 10 kDa to about 16 kDa.
8. A conjugate as claimed in any of claims 1 to 7, wherein the targeting agent comprises less than 120 amino acid residues.
9. A conjugate as claimed in any of claims 1 to 8, wherein the targeting agent comprises or consists of any of the amino acid sequences as defined herein.
10. A conjugate as claimed in any of claims 1 to 9, wherein one targeting agent is covalently linked to the dendrimer.
11. A conjugate as claimed in any of claims 1 to 9, wherein more than one targeting agent is covalently linked to the dendrimer.
12. A conjugate as claimed in any of claims 1 to 11, wherein the covalent linkage between the targeting agent and the spacer group has been formed by reaction between complementary reactive functional groups present on a targeting agent precursor and a spacer group precursor.
13. A conjugate as claimed in claim 12, wherein the targeting agent precursor comprises an unnatural amino acid residue, the unnatural amino acid residue having a side-chain including a reactive functional group.
14. A conjugate as claimed in claim 13, wherein the unnatural amino acid residue is a residue of



15. A conjugate as claimed in any of claims 1 to 14, wherein the targeting agent is covalently linked to the spacer group *via* the C-terminus of the targeting agent.

16. A conjugate as claimed in any of claims 12 to 15, wherein the spacer group precursor
5 comprises a reactive functional group which is an alkyne group.

17. A conjugate as claimed in claim 16, wherein the alkyne group is a dibenzocyclooctyne group.

10 18. A conjugate as claimed in any one of claims 1 to 15, wherein the therapeutic agent is a chemotherapeutic agent.

19. A conjugate as claimed in any one of claims 1 to 18, wherein the therapeutic agent is a cytotoxic agent.

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20. A conjugate as claimed in any one of claims 1 to 19, wherein the therapeutic agent is an ultracytotoxic agent.

21. A conjugate as claimed in claim 20, wherein the therapeutic agent is an auristatin or a
20 maytansinoid.

22. A conjugate as claimed in claim 21, wherein the therapeutic agent is monomethyl auristatin E.

25 23. A conjugate as claimed in claim 21, wherein the therapeutic agent is monomethyl auristatin F.

24. A conjugate as claimed in any of claims 1 to 23, wherein the therapeutic agent is covalently linked to a surface building unit of the dendrimer *via* a linker.

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25. A conjugate as claimed in any of claims 1 to 24, wherein the therapeutic agent is covalently linked to a surface building unit of the dendrimer *via* a cleavable linker.

26. A conjugate as claimed in claim 25, wherein the cleavable linker comprises either a Val-Cit-PAB group or a Val-Arg-PAB-P-Trigger group.

27. A conjugate as claimed in any of claims 1 to 26, wherein the hydrophilic polymeric group is selected from the group consisting of polyethylene glycol (PEG), polyethyloxazoline (PEOX), or polysarcosine.

28. A conjugate as claimed in any of claims 1 to 27, wherein the conjugate comprises PEG groups that are covalently linked to surface building units of the dendrimer.

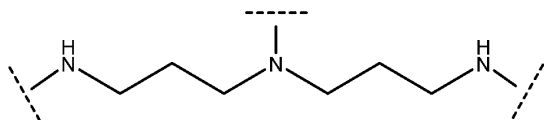
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29. A conjugate as claimed in claim 28, wherein the PEG groups have an average molecular weight in the range of from about 500 to about 2500 g/mole.

30. A conjugate as claimed in any of claims 1 to 29, wherein the spacer group comprises a PEG group.

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31. A conjugate as claimed in any of claims 1 to 30, wherein the core unit comprises the structure:



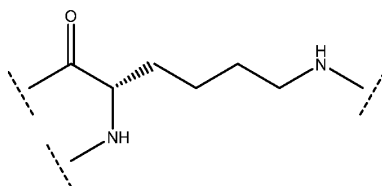
32. A conjugate as claimed in any of claims 1 to 31, wherein the dendrimer has from one to five generations of building units.

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33. A conjugate as claimed in claim 32, wherein the dendrimer has three generations of building units.

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34. A conjugate as claimed in any of claims 1 to 33, wherein the building units are each:



35. A conjugate as claimed in any of claims 1 to 34, for administration in combination with a further active agent.

36. A conjugate as claimed in any of claims 1 to 35, wherein the conjugate is internalised
5 within a HER2-expressing cell.

37. A conjugate as claimed in any one of claims 1 to 36, wherein administration of the conjugate results in reduced side effects in comparison to administration of an equivalent dose of free therapeutic agent.

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38. A conjugate as claimed in any of claims 1 to 37, wherein administration of the conjugate results in at least a 50% reduction in the maximum plasma concentration of released therapeutic agent in comparison to administration of an equivalent dose of free therapeutic agent.

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39. A composition comprising a plurality of conjugates as defined in any of claims 1 to 38.

40. A pharmaceutical composition, comprising:

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- i) a conjugate as claimed in any of claims 1 to 39; and
- ii) a pharmaceutically acceptable excipient.

41. A composition as claimed in claim 39 or 40, wherein the composition is formulated for parenteral delivery.

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42. A conjugate as claimed in any of claims 1 to 38, or a composition as claimed in any of claims 39 to 41, for use in the treatment of cancer.

43. A method of treating cancer comprising administering to a subject in need thereof a
30 therapeutically effective amount of a conjugate as claimed in any of claims 1 to 38 or a composition as claimed in any of claims 39 to 42.

44. Use of a conjugate as claimed in any of claims 1 to 38, or of a composition as claimed in any of claims 39 to 43, in the manufacture of a medicament for the treatment of cancer.

45. A method, use, or conjugate or composition for use, as claimed in any of claims 42 to 44, wherein the cancer is ovarian cancer, breast cancer, stomach cancer, uterine cancer, or another cancer characterised by abnormal expression of the ERBB2 gene.

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46. A method of killing a HER2-expressing cell, comprising:
contacting a conjugate as claimed in any of claims 1 to 38 with a HER2-expressing cell such that the conjugate is internalised within the cell, whereby the therapeutic agent kills the HER2-expressing cell.