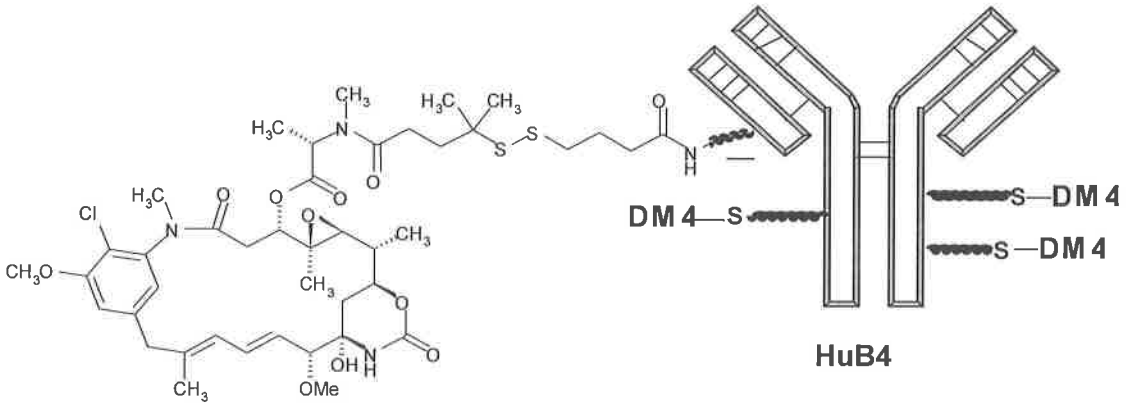
CLAIMS

1. ~~A method of treating CD19+ B-cell malignancies symptom in a patient in need thereof, said method comprising administering to said patient therapeutically effective amounts of~~ Use of an anti-CD19 maytansinoid immunoconjugate in the manufacture of a medicament for the treatment of leukemia or lymphoma, wherein said anti-CD19 maytansinoid immunoconjugate:

i. has the following formula:



and

ii. comprises an antibody comprising a light chain and a heavy chain, said light chain having the sequence of SEQ ID NO: 7, and said heavy chain having the sequence of SEQ ID NO: 8.

2. ~~An method~~The use according to claim 1, wherein the immunoconjugate is to be administered with a dose regimen reducing the toxicity resulting from the treatment.

3. ~~A method~~The use according to ~~any one of~~ claim~~s 1 and~~ 2, wherein the toxicity is an ocular toxicity resulting in eye related adverse events.

4. ~~A method~~ The use according to claim 3, wherein the occurrence all grades of eye related adverse events is below 40 %.

5. ~~A method~~ The use according to claim 3, wherein the occurrence of eye related adverse events grade 3 or 4 is below 13 %.

6. The use according to any one of claims 1 to 5, wherein said anti-CD19 maytansinoid immunoconjugate is to be administered at a dose of about 55 mg/m^2.

~~6. A method of treating CD19+ B-cell malignancies symptom in a patient in need thereof, said method comprising the steps of administering to the patient an initial dose of about 55 mg/m² of the anti-CD19 maytansinoid immunoconjugate; and administering to the patient a plurality of subsequent doses of about 55 mg/m² of the anti-CD19 maytansinoid immunoconjugate, wherein the subsequent doses are separated in time from each other by about one week.~~

~~7. A method according to claim 6 wherein the administration of the initial dose is followed by the administration of at least 6 doses separated in time from each other by about one week.~~

~~8. A method according to any one of claims 6 and 7 wherein the administration of the initial dose is followed by the administration of between 6 and 14 doses separated in time from each other by about one week.~~

~~9. A method according to any one of claims 6 and 7 wherein said method comprises the steps of:~~

- ~~administering to the patient an initial dose of about 55 mg/m², of the anti-CD19 maytansinoid immunoconjugate, and~~

- ~~administering to the patient at least 6 subsequent doses of about 55 mg/m² separated in time from each other by about one week of the anti-CD19.~~

~~10. A method according to claim 6 wherein said method comprises a further step of administration of subsequent doses of about 55 mg/m² of anti-CD19 maytansinoid immunoconjugate wherein the doses are separated in time from each other by about two weeks.~~

~~11~~7. ~~A method according to any one of claims 6 and 10 wherein said method comprises the steps of~~ Use of an anti-CD19 maytansinoid immunoconjugate in the manufacture of a medicament for the treatment of leukemia or lymphoma in a patient, wherein said anti-CD19 maytansinoid immunoconjugate is to be administered with the following dosage regimen:

(a) administration ~~ering to the patient~~of an initial dose of about 55 mg/m², ~~of the anti-CD19 maytansinoid immunoconjugate~~,

(b) administration~~ering to the patient~~of at least 3 subsequent doses of about 55 mg/m² separated in time from each other by about one week ~~of the anti-CD19 maytansinoid immunoconjugate~~, and

(c) administration ~~ering to the patient~~of at least 3 subsequent doses of about 55 mg/m² of the anti-CD19 maytansinoid immunoconjugate, separated in time from each other by about two weeks.

8. The use according to claim 7, wherein step (b) consists in the administration of 3 subsequent doses.

9. The use according to claim 7, wherein step (c) consists in the administration of 3 subsequent doses.

~~12. A method according to any one of claims 1 to 11 wherein said CD19+ B-cell malignancies symptom is a leukemia symptom or a lymphoma symptom.~~

~~13~~10. The use~~A method~~ according to any one of claims ~~12~~ 7 to 9, wherein said ~~leukemia symptom~~lymphoma is a Non-Hodgkin's lymphoma ~~symptom~~ (NHL) ~~symptom~~.

~~14. A method according to claim 12 wherein said lymphoma symptom is Acute lymphoblastic leukemia (ALL) symptom.~~

~~15~~11. The use ~~A method~~ according to claim ~~13~~ 10; wherein said Non-Hodgkin's lymphoma ~~symptom~~ is selected from the group consisting of a Diffuse Large B-cell lymphoma (DLBCL), a folicullar lymphoma (FL), a Mantle cell lymphoma (MCL), a Marginal zone lymphoma

(MZL), a Small lymphocytic lymphoma (SLL) ~~or~~ and a Waldenström macroglobulinemia (WM).

12. The use according to claim 11, wherein said Non-Hodgkin's lymphoma is a Diffuse Large B-cell lymphoma (DLBCL).

~~16~~13. The use~~A method~~ according to claim ~~13~~ 10, wherein said Non-Hodgkin's lymphoma ~~symptom~~ is a relapsed or refractory B-cell non-Hodgkin's lymphoma.

~~17~~14. The use ~~A method~~ according to claim ~~13~~ 10, wherein said Non-Hodgkin's lymphoma ~~symptom~~ is a B-cell non-Hodgkin's lymphoma expressing CD19.

~~18. A method according to claim 13 wherein said patient has already been treated for the Non-Hodgkin's lymphoma symptom.~~

~~19. A method according to claim 13 wherein said patient has failed rituximab therapy.~~

~~20. A method according to claim 13 wherein said Non-Hodgkin's lymphoma symptom is a rituximab resistant disease.~~

~~21. A method according t to claim 13 wherein said patient has received an autologous or allogeneic stem cell transplant.~~

~~22. A method according to any one of claims 1 to 21 wherein the anti-CD19 maytansinoid immunoconjugate is administered intravenously.~~

~~23. A method according to any one of claims 1 to 22 which is safe and effective.~~

~~24~~15. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~23~~ 14, which further comprises ~~administering~~ simultaneous~~ly~~ or sequential~~ly~~ administration of an effective amount of a chemotherapeutic agent.

~~25. A method according to any one of claims 1 to 24 wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody which binds specifically to the CD19 antigen conjugated to a cytotoxic of the maytansinoid family.~~

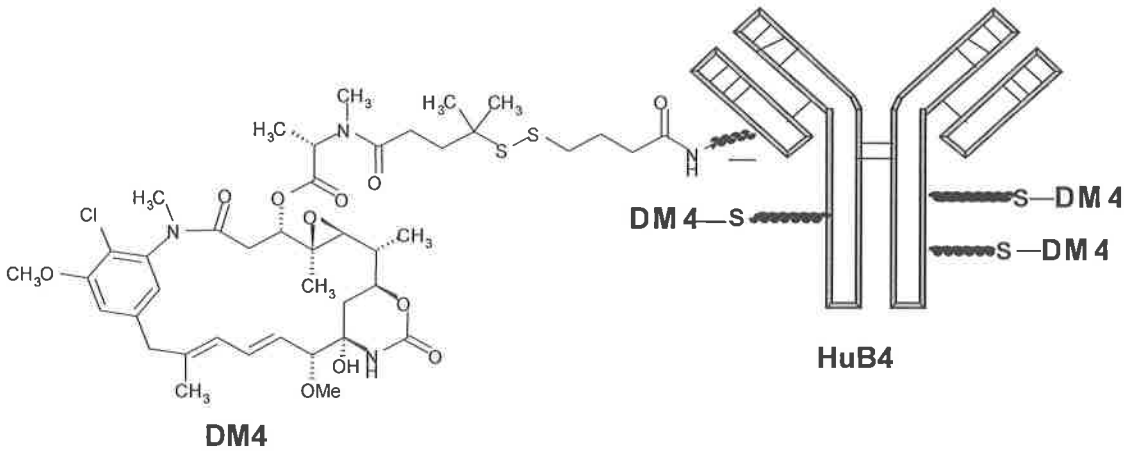
~~26~~16. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~25~~ 15, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody which binds specifically to the CD19 antigen conjugated to DM4.

~~27~~17. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~26~~ 16, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody which binds specifically to the CD19 antigen conjugated to DM4 through a cleavable linker.

~~28~~18. The use~~A method~~ according to any one of claims ~~1~~ 7 to ~~27~~ 17, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody which binds specifically to the CD19 antigen conjugated to DM4 through a N-succinimidyl 4-(2-pyridyldithio)butanoate (SPDB) linker.

2919. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~28~~ 18, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody which binds specifically to the CD19 antigen conjugated to DM4 through N-succinimidyl 4-(2-pyridyldithio)butanoate (SPDB) linker, wherein about 3.5 molecules of DM4 are bound through the SPDB linker to each huB4 molecule.

3020. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~29~~ 19, wherein the anti-CD19 maytansinoid immunoconjugate has the following formula:



3121. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~30~~ 20, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody and the said antibody comprises six complementary determining region (CDR), said CDR having the sequences represented in SEQ ID NOs 1 to 6.

3222. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~30~~ 20, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody and the said antibody comprises a light chain, wherein the sequence of the said light chain has at least 60%, identity with the sequence displayed in SEQ ID NO. 7.

3323. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~30~~ 20, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody and the said antibody comprises a heavy chain, wherein the sequence of the said heavy chain has at least 60%, identity with the sequence displayed in SEQ ID NO. 8.

~~34~~24. The use ~~A method~~ according to any one of claims ~~1~~ 7 to ~~30~~20, wherein the anti-CD19 maytansinoid immunoconjugate comprises an antibody and the said antibody comprises a light chain and a heavy chain, said light chain having the sequence represented in SEQ ID NO. 7, and said heavy chain having the sequence represented in SEQ ID NO. 8.

~~35. A method according to any one of claims 1 to 30 wherein the anti-CD19 maytansinoid immunoconjugate comprises the HuB4 antibody.~~

~~36. A method according to any one of claims 1 to 30 wherein the anti-CD19 maytansinoid immunoconjugate is the HuB4-DM4 conjugate.~~

~~37. A method according to any one of claims 2 to 30 wherein the dose regimen reduces the toxicity resulting form the treatment with the HuB4-DM4 conjugate.~~

~~38. Anti-CD19 maytansinoid immunoconjugate for treating a human patient diagnosed with a CD19+ cell malignancy symptom with a method comprising the steps of administering to the patient an initial dose of about 55 mg/m² of the anti-CD19 maytansinoid immunoconjugate; and administering to the patient a plurality of subsequent doses of about 55 mg/m², of the anti-CD19 maytansinoid immunoconjugate, wherein the subsequent doses are separated in time from each other by about one week.~~

~~39. Anti-CD19 maytansinoid immunoconjugate for treating a human patient diagnosed with a CD19+ cell malignancy symptom with a method comprising the steps of administering to the patient an initial dose of about 55 mg/m² of the anti-CD19 maytansinoid immunoconjugate; and then administering to the patient a plurality of subsequent doses of about 55 mg/m², of the anti-CD19 maytansinoid immunoconjugate separated in time from each other by about one week, and in a further step administeriong plurality of subsequent doses of about 55 mg/m² of the anti-CD19 maytansinoid immunoconjugate separated in time from each other by about two weeks.~~

~~40. An article of manufacture comprising:~~

~~a) a packaging material~~

~~b) an anti-CD19 maytansinoid immunoconjugate, and~~

~~c) a label or package insert contained within said packaging material indicating that said anti-CD19 maytansinoid immunoconjugate is administered to the patient at an initial dose of about 55 mg/m², and in a plurality of subsequent doses separated in time from each other by about one week in an amount that is about 55 mg/m².~~

~~41. An article of manufacture comprising:~~

~~a) a packaging material~~

~~b) an anti-CD19 maytansinoid immunoconjugate, and~~

~~c) a label or package insert contained within said packaging material indicating that said anti-CD19 maytansinoid immunoconjugate is administered to the patient at an initial dose of about 55 mg/m², then in a plurality of subsequent doses separated in time from each other by about one week in an amount that is about 55 mg/m² and then in a plurality of subsequent doses separated in time from each other by about two weeks in an amount that is about 55 mg/m².~~

~~42. An article of manufacture comprising:~~

~~a) a packaging material~~

~~b) an anti-CD19 maytansinoid immunoconjugate, and~~

~~c) a label or package insert contained within said packaging material indicating that said anti-CD19 maytansinoid immunoconjugate is administered to the patient at a dose of about 55 mg/m² to minimize the risks of toxicity~~

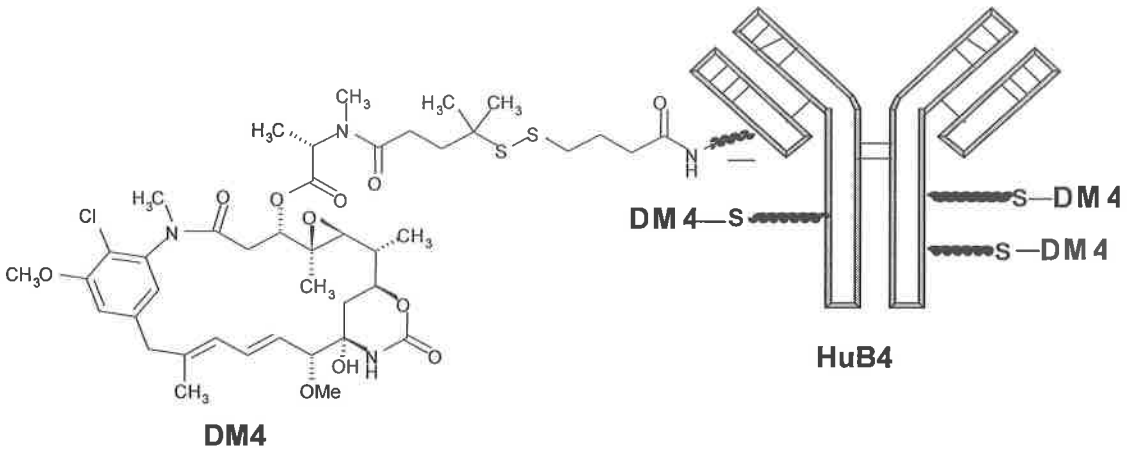
~~43. An article of manufacture according to claim 42 wherein the occurrence of eye related adverse events (all grades) is below 40 %.~~

~~44. An article of manufacture according to claim 42 wherein the occurrence of eye related adverse events grade 3/4 is below 13%.~~

25. An antibody–drug conjugate composed of a humanized IgG1 monoclonal antibody specifically targeting the CD19 antigen conjugated through a disulfide link to the maytansinoid derivative DM4, wherein:

(a) said antibody antibody–drug conjugate has the structure shown in Formula (I); and

Formula (I)



(b) said humanized IgG1 monoclonal antibody specifically targeting the CD19 antigen comprises a light chain having the sequence represented in SEQ ID NO. 7, and a heavy chain having the sequence represented in SEQ ID NO. 8.