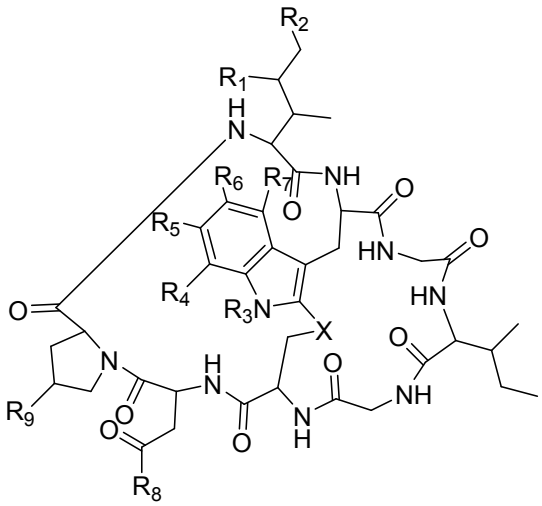
CLAIMS

1. Use of an effective amount of a conjugate comprising an anti-CD117 antibody, or an antigen-binding fragment thereof, and an amatoxin, in the manufacture of a medicament for depleting a population of CD117+ cells wherein the antibody, or the antigen-binding fragment thereof, is internalized by a CD117+ cell.

2. The use of claim 1, wherein the amatoxin is selected from the group consisting of, α-amanitin, β-amanitin, γ-amanitin, ε-amanitin, amanin, amaninamide, amanullin, amanullinic acid, and proamanullin.

3. The use of claim 1, wherein the amatoxin is represented by formula (I)



wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

when present, R_A and R_B, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or -SO_2-;

R_C is -L-Z;

R_D is C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, C_2-C_6 heteroalkenyl, C_2-C_6 alkynyl, C_2-C_6 heteroalkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

L is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, cycloalkylene, heterocycloalkylene, arylene, or heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein the amatoxin comprises one R_C substituent.

4. The use of any one of claims 1 to 3, wherein the antibody, or the antigen-binding fragment thereof, is conjugated to the amatoxin by way of a cysteine residue in the Fc domain of the antibody or antigen-binding fragment thereof.

5. The use of claim 4, wherein the cysteine residue is introduced by way of a mutation in the Fc domain of the antibody or antigen-binding fragment thereof.

6. The use of claim 5, wherein the cysteine residue is selected from the group consisting of Cys118, Cys239, and Cys265.

7. The use of claim 4, wherein the cysteine residue is naturally occurring in the Fc domain of the antibody, or the antigen-binding fragment thereof.

8. The use of claim 7, wherein the Fc domain is a human IgG1 Fc domain and the cysteine residue is selected from the group consisting of Cys261, Csy321, Cys367, and Cys425.

9. The use of any one of claims 1 to 8, wherein the population of CD117+ cells comprises hematopoietic stem cells.

10. The use of any one of claims 1 to 9, wherein the antibody, or the antigen-binding fragment thereof, binds CD117 with a K_d of from about 0.1 pM to about 1 μM.

11. The use of any one of claims 1 to 9, wherein the antibody, or the antigen-binding fragment thereof, binds CD117 with a k_{on} of from about 9 x 10^{-2} $M^{-1}s^{-1}$ to about 1 x 10^{-2} $M^{-1}s^{-1}$.

12. The use of any one of claims 1 to 11, wherein the antibody, or the antigen-binding fragment thereof, competitively inhibits the binding of CD117 to a second antibody comprising the following complementarity determining regions (CDRs):

a CDR-H1 having the amino acid sequence SYWIG (SEQ ID NO: 1);
a CDR-H2 having the amino acid sequence IIYPGDSDTRYSPSFQG (SEQ ID NO: 2);
a CDR-H3 having the amino acid sequence HGRGYNGYEGAFDI (SEQ ID NO: 3);
a CDR-L1 having the amino acid sequence RASQGISSALA (SEQ ID NO: 4);
a CDR-L2 having the amino acid sequence DASSLES (SEQ ID NO: 5); and
a CDR-L3 having the amino acid sequence CQQFNSYPLT (SEQ ID NO: 6).

13. The use of any one of claims 1 to 12, wherein the antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a humanized antibody, a bispecific antibody, and a dual-variable immunoglobulin domain.

14. The use of any one of claims 1 to 12, wherein the antigen-binding fragment is selected from the group consisting of a single-chain Fv molecule (scFv), a diabody, a triabody, a nanobody, a Fv fragment, a Fab fragment, a $F(ab')_2$ molecule, a domain antibody, and a tandem di-scFV.

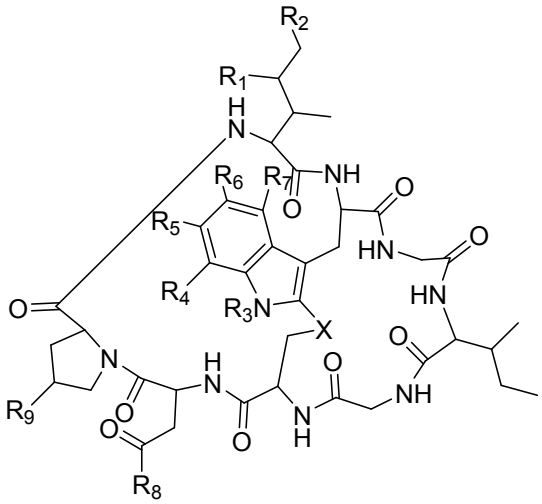
15. Use of an effective amount of a conjugate comprising an anti-CD117 antibody, or an antigen-binding fragment thereof, covalently conjugated to an amatoxin, in the manufacture of a medicament for conditioning prior to a hematopoietic stem cell (HSC) transplantation for a hematological cancer,

wherein the antibody, or the antigen-binding fragment thereof, is internalized by a CD117+ cell

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16. The use of claim 15, wherein the amatoxin is selected from the group consisting of, α-amanitin, β-amanitin, γ-amanitin, ε-amanitin, amanin, amaninamide, amanullin, amanullinic acid, and proamanullin.

17. The use of claim 15, wherein the amatoxin is represented by formula (I)



wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

when present, R_A and R_B, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or -SO_2-;

R_C is -L-Z;

R_D is C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, C_2-C_6 heteroalkenyl, C_2-C_6 alkynyl, C_2-C_6 heteroalkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

L is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, cycloalkylene, heterocycloalkylene, arylene, or heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein the amatoxin comprises one R_C substituent.

18. The use of any one of claims 15 to 17, wherein the conjugate comprises an anti-CD117 IgG antibody covalently conjugated to the amatoxin.

19. The use of any one of claims 15 to 18, wherein the anti-CD117 antibody, or antigen binding fragment thereof, is conjugated to the amatoxin by way of a cysteine residue in the Fc domain of the antibody, or the antigen-binding fragment thereof.

20. The use of any one of claims 15 to 19, wherein the hematological cancer is selected from the group consisting of acute myeloid leukemia, acute lymphoid leukemia, chronic myeloid leukemia, chronic lymphoid leukemia, multiple myeloma, diffuse large B-cell lymphoma, and nonHodgkin's lymphoma.

21. The use of any one of claims 15 to 19, wherein the cancer is leukemia.

22. The use of any one of claims 15 to 21, wherein a population of endogenous CD117+ cells are depleted following administration of the conjugate.

23. The use of claim 22, wherein the CD117+ cells are HSCs.

24. The use of any one of claims 15 to 23, further comprising administering an HSC transplant.

25. The use of any one of claims 15 to 24, wherein the anti-CD117 antibody or antigen binding fragment thereof binds CD117 with a K_d of from about 0.1 pM to about 1 μM.

26. The use of any one of claims 15 to 24, wherein the antibody or antigen-binding fragment thereof binds CD117 with a k_{on} of from about 9×10^{-2} M^{-1} s^{-1} to about 1×10^{2} M^{-1} s^{-1}.

27. The use of any one of claims 15 to 26, wherein the anti-CD117 antibody or antigen binding fragment thereof competitively inhibits the binding of CD117 to a second anti-CD117 antibody comprising the following CDRs:

a CDR-H1 having the amino acid sequence SYWIG (SEQ ID NO: 1);
a CDR-H2 having the amino acid sequence IIYPGDSDTRYSPSFQG (SEQ ID NO: 2);
a CDR-H3 having the amino acid sequence HGRGYNGYEGAFDI (SEQ ID NO: 3);
a CDR-L1 having the amino acid sequence RASQGISSALA (SEQ ID NO: 4);
a CDR-L2 having the amino acid sequence DASSLES (SEQ ID NO: 5); and
a CDR-L3 having the amino acid sequence CQQFNSYPLT (SEQ ID NO: 6)**.**

28. The use of any one of claims 15 to 27, wherein the anti-CD117 antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a humanized antibody, a bispecific antibody, and a dual-variable immunoglobulin domain.

29. Use of an effective amount of a conjugate, wherein the conjugate comprises an anti-CD117 antibody, or an antigen-binding fragment thereof, covalently conjugated to an amatoxin, in the manufacture of a medicament for conditioning a human patient for receiving a hematopoietic stem cell (HSC) transplantation, wherein the human patient has a hematological cancer, and wherein the antibody, or the antigen-binding fragment thereof, is internalized by a CD117+ cell.