

Claims:

1. A method of treating a CD30-positive cancer in a subject, comprising:
(i) administering a lymphodepleting chemotherapy to the subject, and
5 (ii) subsequently administering CD30-specific chimeric antigen receptor (CAR)-expressing T cells to the subject.
2. A population of CD30-specific chimeric antigen receptor (CAR)-expressing T cells for use in a method of treating a CD30-positive cancer, wherein the method comprises:
10 (i) administering a lymphodepleting chemotherapy to the subject, and
(ii) subsequently administering CD30-specific CAR-T cells to the subject.
3. Use of a population of CD30-specific chimeric antigen receptor (CAR)-expressing T cells in the manufacture of a medicament for use in a method of treating a CD30-positive cancer, wherein the
15 method comprises:
(i) administering a lymphodepleting chemotherapy to the subject, and
(ii) subsequently administering CD30-specific CAR-T cells to the subject.
4. The method according to claim 1, the population for use according to claim 2, or the use according to
20 claim 3, wherein administering a lymphodepleting chemotherapy to the subject comprises administering fludarabine and bendamustine.
5. The method, the population for use or the use according to any one of claims 1 to 4, wherein the method comprises administering fludarabine at a dose of 15 to 60 mg/m² per day, for 2 to 6 consecutive
25 days.
6. The method, the population for use or the use according to any one of claims 1 to 5, wherein the method comprises administering fludarabine at a dose of 30 mg/m² per day, for 3 consecutive days.
- 30 7. The method, the population for use or the use according to any one of claims 1 to 6, wherein the method comprises administering bendamustine at a dose of 35 to 140 mg/m² per day, for 2 to 6 consecutive days.
8. The method, the population for use or the use according to any one of claims 1 to 7, wherein the
35 method comprises administering bendamustine at a dose of 70 mg/m² per day, for 3 consecutive days.
9. The method, the population for use or the use according to any one of claims 1 to 8, wherein the method comprises administering 5×10^7 CD30-specific CAR-expressing T cells/m² to 1×10^9 CD30-specific CAR-expressing T cells/m² to the subject.
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10. The method, the population for use or the use according to any one of claims 1 to 9, wherein the method comprises administering 1×10^8 CD30-specific CAR-expressing T cells/m² to 6×10^8 CD30-specific CAR-expressing T cells/m² to the subject.
- 5 11. The method, the population for use or the use according to any one of claims 1 to 10, wherein the method comprises:
- (i) administering fludarabine at a dose of 30 mg/m² per day and bendamustine at a dose of 70 mg/m² per day to a subject for 3 consecutive days, and
 - (ii) subsequently administering CD30-specific CAR-expressing T cells to the subject at a dose of
- 10 2×10^8 CD30-specific CAR-expressing T cells/m² to 6×10^8 CD30-specific CAR-expressing T cells/m².
12. The method, the population for use or the use according to any one of claims 1 to 11, wherein the CD30-positive cancer is selected from: a hematological cancer, a solid cancer, a hematopoietic malignancy, Hodgkin's lymphoma, anaplastic large cell lymphoma, peripheral T cell lymphoma, peripheral
- 15 T cell lymphoma not otherwise specified, T cell leukemia, T cell lymphoma, cutaneous T cell lymphoma, NK-T cell lymphoma, extranodal NK-T cell lymphoma, non-Hodgkin's lymphoma, B cell non-Hodgkin's lymphoma, diffuse large B cell lymphoma, diffuse large B cell lymphoma not otherwise specified, EBV-positive B cell lymphoma, EBV-positive diffuse large B cell lymphoma, primary mediastinal B cell lymphoma, advanced systemic mastocytosis, a germ cell tumor and testicular embryonal carcinoma.
- 20 13. The method, the population for use or the use according to any one of claims 1 to 12, wherein the CD30-positive cancer is selected from: Hodgkin's lymphoma, non-Hodgkin's lymphoma, anaplastic large cell lymphoma, peripheral T cell lymphoma not otherwise specified, extranodal NK-T cell lymphoma, diffuse large B cell lymphoma not otherwise specified and primary mediastinal large B-cell lymphoma.
- 25 14. The method, the population for use or the use according to any one of claims 1 to 13, wherein the subject has previously failed therapy for the CD30-positive cancer.
15. The method, the population for use or the use according to any one of claims 1 to 14, wherein the
- 30 CD30-positive cancer is a relapsed or refractory CD30-positive cancer.
16. The method, the population for use or the use according to any one of claims 1 to 15, wherein CD30-specific CAR-expressing T cells comprise a CAR comprising: (i) an antigen-binding domain which binds specifically to CD30, (ii) a transmembrane domain, and (iii) a signalling domain, wherein the signalling
- 35 domain comprises: (a) an amino acid sequence derived from the intracellular domain of CD28, and (b) an amino acid sequence comprising an immunoreceptor tyrosine-based activation motif (ITAM).
17. The method, the population for use or the use according to claim 16, wherein the signalling domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:26.
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18. The method, the population for use or the use according to claim 16 or claim 17 wherein the transmembrane domain is derived from the transmembrane domain of CD28.
19. The method, the population for use or the use according to any one of claims 16 to 18, wherein the transmembrane domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:20.
20. The method, the population for use or the use according to any one of claims 16 to 19, wherein the antigen-binding domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:14, and an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:15.
21. The method, the population for use or the use according to any one of claims 16 to 20, wherein the antigen-binding domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:18.
22. The method, the population for use or the use according to any one of claims 16 to 21, wherein the signalling domain comprises: (a) an amino acid sequence derived from the intracellular domain of CD3ζ.
23. The method, the population for use or the use according to any one of claims 16 to 22, wherein the signalling domain comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:25.
24. The method, the population for use or the use according to any one of claims 16 to 23, wherein the CAR additionally comprises a hinge region provided between the antigen-binding domain and the transmembrane domain.
25. The method, the population for use or the use according to any one of claims 16 to 24, wherein the hinge region comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:33.
26. The method, the population for use or the use according to any one of claims 16 to 25, wherein the CAR comprises an amino acid sequence having at least 80% amino acid sequence identity to SEQ ID NO:35 or 36.