

to about 360×10^6 cells/dose, for example about 20×10^6 cells/dose, about 40×10^6 cells/dose, about 80×10^6 cells/dose, about 120×10^6 cells/dose, 240×10^6 cells/dose, or about 360×10^6 cells/dose.

[0009a] In one aspect, the present disclosure refers to use of at least one unit dose of allogeneic chimeric antigen receptor (CAR)-T cells (CAR-T cells) comprising an anti-human CD19 4-1BB/CD3zeta CAR in the manufacture of a medicament for treating a subject who has refractory and/or relapsed Non-Hodgkin's Lymphoma, wherein the at least one unit dose is a unit dose of selected from the group consisting of about 120×10^6 cells/dose, about 240×10^6 cells/dose, and or about 360×10^6 cells/dose, and further wherein the CAR-T cells comprise the CAR of SEQ ID NO: 1.

[0010] In some examples, the methods involve (a) administering to a subject with a disease a first dose of allogeneic CAR-T cells; and (b) administering to the subject a subsequent dose of allogeneic CAR-T cells. In other examples, the methods are carried out by administering to the subject the subsequent dose or doses as in (b), to a subject that has been previously administered the first dose as in (a). In some examples, the CAR-T cells are tumor antigen-specific CAR-T cells. In some examples, the CAR-T cells are CD19-specific CAR-T cells (e.g., UCART19 (CD19CAR/RQR8+_{TCRαβ}-T-cells)). In some examples, the disease is a tumor. In some examples, it is a cancer, malignancy, neoplasm, or other proliferative disease or disorder, such as leukemia, lymphoma, e.g., chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL (e.g., relapsed/refractory ALL)), non-Hodgkin's lymphoma, acute myeloid leukemia, diffuse large B-cell lymphoma (DLBCL), multiple myeloma, follicular lymphoma, mantle cell lymphoma, indolent B cell lymphoma, B cell malignancies, cancers of the colon, lung (e.g., small and non-small cell lung cancer), liver, breast, prostate, ovarian, skin, melanoma, bone, and brain cancer, ovarian cancer, epithelial cancers, renal cell carcinoma, pancreatic adenocarcinoma, Hodgkin lymphoma, cervical carcinoma, colorectal cancer, glioblastoma, neuroblastoma, Ewing sarcoma, medulloblastoma, osteosarcoma, synovial sarcoma, head and neck squamous cell carcinoma (HNSCC), and/or mesothelioma. In some examples, the disease is a leukemia or lymphoma. In some examples, the disease is acute lymphoblastic leukemia. In some examples, the disease is relapsed or refractory acute lymphoblastic leukemia. In some examples, the disease is non-Hodgkin lymphoma (NHL). In some examples, the disease is relapsed or refractory large B-cell lymphoma. In some examples, the disease is relapsed or refractory follicular lymphoma.

[0011] In some examples the disease is acute lymphoblastic leukemia (ALL). In some examples the disease is pediatric acute lymphoblastic leukemia (ALL). In some examples the disease is an advanced lymphoid malignancy such as B-cell acute lymphoblastic leukemia (B-ALL). In some examples, the disease is refractory B-ALL, e.g. adult refractory B-ALL. In some examples, the disease is relapsed B-ALL, e.g. adult relapsed B-ALL. In some examples, the disease is extramedullary disease associated, for example, with one or more of the cancers described herein. In some examples, the subject exhibits detectable molecular

CLAIMS

1. Use of at least one unit dose of allogeneic chimeric antigen receptor (CAR)-T cells (CAR-T cells) comprising an anti-human CD19 4-1BB/CD3zeta CAR in the manufacture of a medicament for treating a subject who has refractory and/or relapsed Non-Hodgkin's Lymphoma, wherein the at least one unit dose is a unit dose of selected from the group consisting of about 120×10^6 cells/dose, about 240×10^6 cells/dose, and or about 360×10^6 cells/dose, and further wherein the CAR-T cells comprise the CAR of SEQ ID NO: 1.
2. The use of claim 1, wherein the Non-Hodgkin's Lymphoma is large B-cell lymphoma.
3. The use of claim 1, wherein the Non-Hodgkin's Lymphoma is follicular lymphoma.
4. The use of any one of claims 1 to 3, wherein the at least one unit dose is about 240×10^6 360×10^6 cells/dose.
5. The use of any one of claims 1 to 3 wherein the at least one unit dose is selected from the group consisting of about 120×10^6 cells/dose, and about 360×10^6 cells/dose.
6. The use of any one of claims 1 to 5, wherein the CAR-T cells are CD52 deficient.
7. The use of any one of claims 1 to 5, wherein the CAR-T cells comprise a mixture of CD52-deficient and CD-52 positive cells.
- ~~8. The use of any one of claims 1 to 7, wherein the CAR-T cells comprise the CAR of SEQ ID NO: 1.~~
- 9.8. The use of any one of claims 1 to 87, wherein the CAR-T cells comprise UCART19(CD19)CAR/RQR8+_TCR $\alpha\beta$ -T-cells.
- ~~10.9.~~ The use of any one of claims 1 to 87, wherein the CAR-T cells do not express a safety switch.
- ~~11.10.~~ The use of any one of claims 1 to 109, wherein CAR expression is detectable in the subject for up to at least 14 days after administration of the CAR-T cells.
- ~~12.11.~~ The use of any one of claims 1 to 110, wherein CAR expression is detectable in the subject for up to at least 28 days after administration of the CAR-T cells.

- ~~13.12.~~ The use of any one of claims ~~1~~1 to ~~12~~11, wherein the subject exhibits a complete response (CR) or complete response with incomplete recovery of blood count (Cri) state for at least 1 months after CAR-T administration.
- ~~14.13.~~ The use of any one of claims 1 to ~~13~~12, wherein the subject exhibits a CR or Cri state for at least 2 months after CAR-T administration.
- ~~15.14.~~ The use of any one of claims 1 to ~~14~~13, wherein the subject exhibits a CR or Cri state for at least 6 months after CAR-T administration.
- ~~16.15.~~ The use of any one of claims 1 to ~~15~~14, wherein the subject exhibits a CR or Cri state for at least 12 months after CAR-T administration.
- ~~17.16.~~ The use of any one of claims 1 to ~~16~~15, wherein the subject receives a first lymphodepletion regimen prior to administration of the at least one unit dose.
- ~~18.17.~~ The use of claim ~~17~~16, wherein the first lymphodepletion regimen comprises administration of fludarabine and cyclophosphamide.
- ~~19.18.~~ The use of claim ~~17~~16, wherein the first lymphodepletion regimen comprises administration of fludarabine, cyclophosphamide, and an anti-CD52 antibody.
- ~~20.19.~~ The use of claim ~~18~~17 or ~~19~~18, wherein the first lymphodepletion regimen further comprises administration of Mensa (sodium-2-mercaptoethanesulfonate).
- ~~21.20.~~ The use of any one of claims ~~18~~17 to ~~20~~19, wherein the first lymphodepletion regimen further comprises administration of at least one corticosteroid.
- ~~22.21.~~ The use of claim ~~21~~20, wherein the corticosteroid is to be administered immediately prior to administration of the anti-CD52 antibody.
- ~~23.22.~~ The use of claim ~~21~~20 or ~~22~~21, wherein the corticosteroid is methylprednisolone.
- ~~24.23.~~ The use of claim ~~23~~22, wherein the methylprednisolone is to be administered at a dose of 2 mg/kg.
- ~~25.24.~~ The use of any one of claims 1 to ~~24~~23, wherein the subject is one that receives a premedication for infusion-related reaction prior to the lymphodepletion regimen.
- ~~26.25.~~ The use of claim ~~25~~24, wherein the premedication comprises at least one antihistamine.

27.26. The use of claim 25-24 or 2625, wherein the premedication comprises acetaminophen.

28.27. The use of any one of claims 18-17 to 2726, wherein fludarabine is to be administered at a dosage of about 30 mg/m²/day; cyclophosphamide is to be administered at a dosage of about 300 mg/m²/day; or CD52 antibody is to be administered at a dosage of 10 mg/day to 13 mg/day or a total dose from about 0.3 mg/kg to about 1 mg/kg, or a flat dose of from about 30 mg to about 40 mg, from about 25 mg to about 60 mg, or from about 100 mg to about 120 mg.

29.28. The use of any one of claims 19-18 to 2726, wherein fludarabine is to be administered at a dosage of about 30 mg/m²/day; cyclophosphamide is to be administered at a dosage of about 300 mg/m²/day; and CD52 antibody is to be administered at a dosage of 10 mg/day to 13 mg/day or a total dose from about 0.3 mg/kg to about 1 mg/kg, or a flat dose of from about 30 mg to about 40 mg, from about 25 mg to about 60 mg, or from about 100 mg to about 120 mg.

30.29. The use of any one of claims 17-16 to 2928, wherein the first lymphodepletion regimen is initiated between 1 to 15 days prior to administration of the at least one unit dose.

31.30. The use of any one of claims 17-16 to 3029, wherein the first lymphodepletion regimen is to be administered over the course of 1, 2, 3, 4, or 5 days.

32.31. The use of any one of claims 1 to 3130, wherein the subject ~~is one that~~ receives a subsequent unit dose of the CAR-T cells.

33.32. The use of claim 3231, wherein the subject exhibits any one of the following at the time of the administration of the subsequent unit dose:

- (a) complete response (CR), complete response with incomplete recovery of blood count (CRi), with detectable minimal residual disease (leukemic patients) and absence of cytogenetic response;
- (b) marrow complete response;
- (c) partial response; or

(d) stable response.

~~34.33.~~ The use of claim ~~32-31~~ or ~~3332~~, wherein the subsequent unit dose comprises about the same number of cells as the number of cells in the at least one unit~~first~~ dose.

~~35.34.~~ The use of claim ~~32-31~~ or ~~3332~~, wherein the subsequent unit dose comprises an increased number of cells as compared to the at least one unit~~first~~ dose.

~~36.35.~~ The use of claim ~~32-31~~ or ~~3332~~, wherein the subsequent unit dose comprises a decreased number of cells as compared to the at least one unit~~first~~ dose.

~~37.36.~~ The use of any one of claims ~~32-31~~ to ~~3635~~, wherein the subsequent unit dose is to be administered at least 14, at least 28, at least 42, or at least 56 days after the at least one unit~~first~~ dose.