Summary

[0005] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, such as a B-ALL or a B-NHL, including a malignancy thereof that is relapsed and/or refractory, the method comprising administering, to a subject at or younger than 25 years of age, or in some cases younger than 18 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR). Such methods and uses include therapeutic methods and uses, for example, involving administration of the anti-CD19 CAR-expressing T cell compositions in an effective amount to effect treatment of the disease or disorder. Uses include uses of such anti-CD19 CAR-expressing in such methods and treatments, and in the preparation of a medicament in order to carry out such therapeutic methods. In some examples, the methods thereby treat the disease or condition or disorder in the subject.

[0006] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount selected from: (i) if the subject is less than 100 kilograms (kg) in body weight and is younger than 18 years of age, from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject; and (ii) if the subject is at or greater than 100 kilograms (kg) in body weight or is between 18 and 25 years of age, inclusive, from at or about 0.05 x 10^8 CAR+ T cells to at or about 1.5 x 10^8 CAR+ T cells. In some of any examples, if the subject is between 18 and 25 years of age, inclusive, the T cell composition is administered in an amount from at or about 0.05 x 10^8 CAR+ T cells to at or about 1.5 x 10^8 CAR+ T cells.

[0007] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method comprising administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount selected from: (i) if the subject is less than 100 kilograms (kg) in body weight and is younger than 18 years of age, from at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject; and (ii) if the subject is at or greater than 100 kilograms (kg) in body weight or is between 18 and 25 years of age, inclusive, from at or about 0.5 x 10^8 CAR+ T cells to at or about 1.5 x 10^8 CAR+ T cells. In some of any examples, if the subject is between 18 and 25 years of age, inclusive, the T cell composition is administered in an amount from at or about 0.5 x 10^8 CAR+ T cells to at or about 1.5 x 10^8 CAR+ T cells.

[0008] In some of any examples, (i) if the subject is less than 100 kilograms (kg) in body weight and is younger than 18 years of age, the T cell composition is administered in an amount from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject; and (ii) if the subject is at or greater than 100 kilograms (kg) in body weight or is

(kg) in body weight, at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject; and (ii) if the subject is at or greater than 100 kilograms (kg) in body weight, at or about 0.75 x 10^8 CAR+ T cells.

[0020] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, involving administering, to a subject that is younger than 18 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is less than 100 kilograms (kg) in body weight, at or about 1.0 x 10^6 CAR+ T cells/kg body weight of the subject; and (ii) if the subject is at or greater than 100 kilograms (kg) in body weight, at or about 1.0 x 10^8 CAR+ T cells.

[0021] Provided herein are methods of treating a subjecting having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells; or (ii) if the subject is between 18 and 25 years of age, inclusive, from at or about 0.05 x 10^8 CAR+ T cells to at or about 1.5 x 10^8 CAR+ T cells.

[0021a] In one aspect, the present disclosure refers to the use of a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR) for the manufacture of a medicament for treatment of a subject at or younger than 25 years of age having or suspected of having a B cell malignancy, wherein the composition is to be administered in an amount selected from: (i) if the subject is younger than 18 years of age, the medicament is formulated for administration of 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, the medicament is formulated for administration of 0.05 x 10^8 CAR+ T cells to 1.5 x 10^8 CAR+ T cells.

[0022] Provided herein are methods of treating a subjecting having or suspected of having a B cell malignancy, the method comprising administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age from at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells; or (ii) if the subject is between 18 and 25 years of age, inclusive, from at or about 0.5 x 10^8 CAR+ T cells to at or about 1.5 x 10^8 CAR+ T cells.

[0023] In some of any examples,: (i) if the subject is younger than 18 years of age, the T cell composition is administered in an amount from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 0.75 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, the T cell composition is administered in an amount from at or about 0.05 x 10^8 CAR+ T cells to at or about 0.75 x 10^8 CAR+ T cells.

[0024] Provided herein are methods of treating a subjecting having or suspected of having a B cell malignancy, involving administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells.

[0025] In some of any examples, the T cell composition is administered in an amount from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 0.75 x 10^8 total CAR+ T cells.

[0026] In some of any examples, the T cell composition is administered in an amount that is at least at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.05 x 10^8 total CAR+ T cells. In some of any examples, if the subject exhibits no response and does not develop a toxicity at or about 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35 days after administration of the T cell composition; further comprising administering to the subject an additional dose of the T cell composition wherein, the additional dose of the T cell composition is administered in an amount that is at least at or about 0.1 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.1 x 10^8 total CAR+ T cells. In some of any examples, the T cell composition is administered in an amount that is at least at or about 0.15 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.15 x 10^8 total CAR+ T cells. In some of any examples, the T cell composition is administered in an amount that is at least at or about 0.3 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.3 x 10^8 total CAR+ T cells. In some of any examples, the T cell composition is administered in an amount that is at least at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.5 x 10^8 total CAR+ T cells. In some of any examples, the T cell composition is administered in an amount that is at least at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.75 x 10^8 total CAR+ T cells. In some of any examples, the T cell composition is administered in an amount that is at least at or about 1.0 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 1.0 x 10^8 total CAR+ T cells.

[0027] In some of any examples, if the subject is younger than 18 years of age the T cell composition is administered in an amount from at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.0 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.0 x 10^8 total CAR+ T cells.

[0028] In some of any examples, if the subject is younger than 18 years of age the T cell composition is administered in an amount from at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.0 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.0 x 10^8 total CAR+ T cells.

[0029] In some of any examples, if the subject is younger than 18 years of age, the T cell composition is administered in an amount that is at least at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.05 x 10^8 total CAR+ T cells. In some of any examples, if the subject exhibits no response and does not develop a toxicity at or about 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35 days after administration of the T cell composition; further comprising administering to the subject an additional dose of the T cell composition wherein, if the subject is younger than 18 years of age, the additional dose of the T cell composition is administered in

antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 0.05 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.05 x 10^8 CAR+ T cells.

[0033] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age and weighing 12 kg or more, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, at or about 0.15 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 0.15 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.15 x 10^8 CAR+ T cells.

[0034] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age and weighing 12 kg or more, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, at or about 0.3 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 0.3 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.3 x 10^8 CAR+ T cells.

[0035] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method comprising administering, to a subject at or younger than 25 years of age and weighing 12 kg or more, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 0.5 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.5 x 10^8 CAR+ T cells.

[0036] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age and weighing 12 kg or more, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 0.75 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.75 x 10^8 CAR+ T cells.

[0037] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age and weighing 12 kg or more, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, at or about 1 x 10^6 CAR+ T cells/kg body weight of the

subject, but not exceeding at or about 1 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 1 x 10^8 CAR+ T cells.

[0038] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method comprising administering, to a subject at or younger than 25 years of age and weighing 6 kg or more, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from (i) if the subject is younger than 18 years of age at or about 1 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 1 x 10^8 total CAR+ T cells; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 1.0 x 10^8 CAR+ T cells.

[0039] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject younger than 18 years of age and weighing 12 kg or more, a composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount that is at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells. In some of any examples, the composition is administered in an amount from at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.0 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.0 x 10^8 total CAR+ T cells.

[0040] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method comprising administering, to a subject younger than 18 years of age and weighing 12 kg or more, a composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the composition is administered in an amount that is at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells. In some of any examples, the composition is administered in an amount from at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 1.0 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.0 x 10^8 total CAR+ T cells.

[0041] In some of any examples, the composition is administered in an amount that is at least at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.05 x 10^8 total CAR+ T cells. In some of any examples, the composition is administered in an amount that is at or about 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to at or about 0.75 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 0.75 x 10^8 total CAR+ T cells. In some of any examples, the composition is administered in an amount that is at least at or about 0.15 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.15 x 10^8 total CAR+ T cells. In some of any examples, the composition is administered in an amount that is at least at or about 0.3 x 10^6 CAR+ T cells/kg body weight of the subject but that does not exceed at or about 0.3 x 10^8 total CAR+ T cells. In some of any examples, the composition is administered in an

[0047] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, involving administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, an amount not exceeding at or about 0.5×10^8 total CAR+ T cells in a volume of at least 0.1 mL; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.5×10^8 CAR+ T cells.

[0048] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, involving administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, an amount not exceeding at or about 0.75×10^8 total CAR+ T cells in a volume of at least 0.1 mL; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.75×10^8 CAR+ T cells.

[0054] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method comprising administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR) at a concentration of at or greater than 2.5 x 10^6 cells/mL, wherein the T cell composition is administered in an amount selected from (i) if the subject is younger than 18 years of age, an amount not exceeding at or about 0.5 x 10^8 total CAR+ T cells in a volume of at least 0.5 mL; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.5 x 10^8 CAR+ T cells.

[0055] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method involving administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR) at a concentration of at or greater than 2.5 x 10^6 cells/mL, wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, an amount not exceeding at or about 0.75 x 10^8 total CAR+ T cells in a volume of at least 0.75 mL; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 0.75 x 10^8 CAR+ T cells.

[0056] Provided herein are methods of treating a subject having or suspected of having a B cell malignancy, the method comprising administering, to a subject at or younger than 25 years of age, a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR) at a concentration of at or greater than 2.5 x 10^6 cells/mL, wherein the T cell composition is administered in an amount selected from: (i) if the subject is younger than 18 years of age, an amount not exceeding at or about 1 x 10^8 total CAR+ T cells in a volume of at least 0.5 mL; and (ii) if the subject is between 18 and 25 years of age, inclusive, at or about 1.0 x 10^8 CAR+ T cells. In some of any examples, a total volume of at least at or about 0.05 mL of the T cell composition is administered. In some of any examples, a total volume of at least at or about 0.1 mL of the T cell composition is administered. In some of any examples, a total volume of at least at or about 0.5 mL of the T cell composition is administered. In some of any examples, a total volume of at least at or about 1.0 mL of the T cell composition is administered.

[0057] In some of any examples, the total volume of the T cell composition administered is at least 0.05 mL. In some of any examples, the total volume of the T cell composition administered is at least 0.1 mL. In some of any of the provided examples, the total volume of the T cell composition administered is at least 1.0 mL. In some of any of the provided examples, the concentration of the T cell composition is greater than at or about 5 x 10^6 cells/mL or is or is about 5 x 10^6 cells/mL In some of any of the provided examples, the concentration of the T cell composition is greater than at or about 10 x 10^6 cells/mL or is or is about 10 x 10^6 cells/mL. In some of any of the provided examples, the concentration of the T cell composition is greater than or greater than about 15 x 10^6 cells/mL or is or is about 15 x 10^6 cells/mL.

[0058] In some of any of the provided examples, the T cell composition comprises $CD4^+$ and $CD8^+$ CAR+ T cells. In some of any examples, the composition comprises a first composition

Claims

WHAT IS CLAIMED:

1. Use of a T cell composition comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR) for the manufacture of a medicament for treatment of a subject at or younger than 25 years of age having or suspected of having a B cell malignancy, wherein the composition is to be administered in an amount selected from:

(i) if the subject is younger than 18 years of age, the medicament is formulated for administration of 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells; and

(ii) if the subject is between 18 and 25 years of age, inclusive, the medicament is formulated for administration of 0.05 x 10^8 CAR+ T cells to 1.5 x 10^8 CAR+ T cells.

2. The use of claim 1, wherein:

(A) (i) if the subject is younger than 18 years of age, the medicament is formulated for administration in an amount 0.5 x 10^6 CAR+ T cells/kg body weight of the subject to 1.5 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed at or about 1.5 x 10^8 total CAR+ T cells; and

(ii) if the subject is between 18 and 25 years of age, inclusive, the medicament is formulated for administration in an amount 0.5 x 10^8 CAR+ T cells to 1.5 x 10^8 CAR+ T cells; or, wherein

(B) (i) if the subject is younger than 18 years of age, the medicament is formulated for administration in an amount 0.05 x 10^6 CAR+ T cells/kg body weight of the subject to 0.75 x 10^6 CAR+ T cells/kg body weight of the subject, but that does not exceed 0.75 x 10^8 total CAR+ T cells; and

(ii) if the subject is between 18 and 25 years of age, inclusive, the medicament is formulated for administration in an amount from 0.05 x 10^8 CAR+ T cells to 0.75 x 10^8 CAR+ T cells.

3. The use of claim 1, wherein the subject is at or younger than 25 years of age and weighing 12 kg or more having or suspected of having a B cell malignancy, wherein :

(i) if the subject is younger than 18 years of age, the medicament is formulated for administration of at or about 0.5 x 10^6 CAR+ T cells/kg body weight of the subject, but not exceeding at or about 0.5 x 10^8 total CAR+ T cells; and

(ii) if the subject is between 18 and 25 years of age, inclusive, the medicament is formulated for administration of at or about 0.5 x 10^8 CAR+ T cells.

4. The use of any of claims 1-3, wherein the subject is at least 6 kg in body weight.

5. The use of any of claims 1-4, wherein a total volume of at least at 0.05 mL, at least at 0.1 mL, at least at 0.5 mL, or at least 1 mL of the T cell composition is to be administered.

6. The use of any of claims 1-5, wherein the concentration of the T cells is at or greater than 2.5 x 10^6 cells/mL.

7. The use of any of claims 1-6, wherein:

(a) a total volume of at least at 0.1 mL at a concentration of at or greater than 2.5 x 10^6 cells/mL of the T cell composition is to be administered;

(b) a total volume of at least at 0.5 mL at a concentration of at or greater than 2.5 x 10^6 cells/mL of the T cell composition is to be administered; or

(c) a total volume of at least at 1 mL at a concentration of at or greater than 2.5 x 10^6 cells/mL of the T cell composition is to be administered.

8. The use of any of claims 1-7, wherein the T cell composition comprises $CD4^+$ and $CD8^+$ CAR+ T cells.

9. The use of claim 8, wherein the composition comprises a first composition comprising one of the CD4+ CAR+ T cells and the CD8+ CAR+ T cells and a second composition comprising the other of the CD4+ CAR+ T cells and the CD8+ CAR+ T cells, optionally

wherein the first composition and the second composition are to be administered separately, further optionally wherein (i) the first composition and the second composition are to be administered simultaneously or (ii) the first composition and the second composition are to be administered sequentially in either order.

10. The use of claim 9, wherein the amount of the T cell composition to be administered comprises a defined ratio of $CD4^+$ CAR^+ T cells to $CD8^+$ CAR^+ T cells, that is or is approximately 1:1 or is between 1:3 and 3:1, optionally wherein the defined ratio is or is approximately 1:1.

11. The use of any of claims 1-10, wherein:

(a) the B cell malignancy is a lymphoma or a leukemia;

(b) the B cell malignancy is relapsed and/or refractory;

(c) the B cell malignancy is a B-cell acute lymphoblastic leukemia (B-ALL), optionally CD19+ B-ALL; and/or

(d) the B cell malignancy is relapsed or refractory (r/r) B-cell Acute Lymphoblastic Leukemia (B-ALL), optionally

wherein the subject with r/r B-ALL has morphological evidence of disease in bone marrow, further optionally wherein the subject has 5% or greater lymphoblast by morphology.

12. The use of claim 11, wherein:

(a) the subject has a B-ALL comprising any of the following: first or greater marrow relapse, any marrow relapse after allogeneic hematopoietic stem cell transplantation (HSCT); primary refractory, optionally not achieving a complete response (CR) or complete response with incomplete blood count recovery (CRi), optionally following 2 or more separate induction regimens; chemo-refractory, optionally not achieving CR/Cri, optionally after 1 cycle of chemotherapy for relapsed leukemia; or is ineligible for allogeneic HSCT;

(b) the B-ALL is minimum residual disease positive (MRD^{+}); and/or

(c) subjects with B-ALL has less than 5% lymphoblast by morphology and/or minimum residual disease positive (MRD+) disease as detected by a validated assay at a frequency of 1 $x10^{-4}$ or greater in bone marrow cells after two lines of therapy.

13. The use of any of claims 1-12, wherein the subject has Philadelphia chromosome positive ALL and is intolerant to or have failed one or more lines of tyrosine-kinase inhibitor (TKI) therapy, or TKI therapy is contraindicated.

14. The use of any of claims 1-11, wherein the B cell malignancy is a B-cell non-Hodgkin lymphoma (B-NHL), optionally CD19+ B-NHL, optionally wherein:

(a) the B cell malignancy is relapsed or refractory (r/r) B-cell non-Hodgkin lymphoma (B-NHL);

(b) the subject has a B-NHL in which there is measurable disease after 1 or more lines of chemotherapy, has failed HSCT, or is ineligible for HSCT; and/or

(c) the B-NHL is diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), or Burkitt's lymphoma (BL).

15. The use of any of claims 1-14, wherein the subject has received a prior therapy targeting CD19, optionally wherein the subject is or has been identified as having cells expressing CD19 or having a CD19-positive disease after completion of the prior therapy targeting CD19.

16. The use of any of claims 1-15, wherein, prior to the administration of the medicament, the subject has been preconditioned with a lymphodepleting therapy comprising the administration of fludarabine and/or cyclophosphamide.

17. The use of claim 16, wherein:

(a) the lymphodepleting therapy comprises administration of cyclophosphamide at 200-400 mg/m^2, optionally at or about 300 mg/m^2, inclusive, and/or fludarabine at 20-40 mg/m^2, optionally 30 mg/m^2, daily for 2-4 days, optionally for 3 days;

(b) the lymphodepleting therapy comprises administration of cyclophosphamide at about 300 mg/m^2 daily for 3 days and fludarabine at about 30 mg/m^2 daily for 3 days;

(c) the cyclophosphamide and fludarabine are to be administered concurrently; and/or

(d) the lymphodepleting therapy is to be administered 2-7 days prior to the administration of the T cell composition.

18. The use of any of claims 1-17, wherein:

(a) the CAR comprises an scFv specific for a human CD19, a transmembrane domain, a cytoplasmic signaling domain derived from a costimulatory molecule, which optionally is or comprises a human 4-1BB, and a cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule, which optionally is or comprises a human CD3zeta signaling domain, and wherein the CAR optionally further comprises a spacer between the transmembrane domain and the scFv.

19. The use of claim 18, wherein (a) the spacer is a polypeptide spacer that comprises or consists of all or a portion of an immunoglobulin hinge, optionally an IgG4 hinge;

(b) the spacer is about 15 amino acids or less, optionally at or about 12 amino acids in length; and/or

(c) the spacer comprises or consists of the sequence of SEQ ID NO: 1, a sequence encoded by SEQ ID NO: 2, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34; and/or

the spacer comprises the formula X_1PPX_2P, where X_1 is glycine, cysteine or arginine and X_2 is cysteine or threonine.

20. The use of claim 18 or claim 19, wherein (a) the cytoplasmic signaling domain derived from a costimulatory molecule comprises SEQ ID NO: 12 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto; and/or

(b) the cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule comprises SEQ ID NO: 13, 14 or 15 having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, and/or

(c) the transmembrane domain comprises the sequence of amino acids set forth in SEQ ID NO: 8 or a sequence of amino acids that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to SEQ ID NO: 8 or the sequence of amino

acids set forth in SEQ ID NO: 9 or a sequence of amino acids having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to SEQ ID NO:9.

21. The use of any of claims 18-20, wherein:

(a) the scFv comprises a variable light (V_L) chain comprising a CDRL1 sequence of RASQDISKYLN (SEQ ID NO: 35), a CDRL2 sequence of SRLHSGV (SEQ ID NO: 36), and a CDRL3 sequence of GNTLPYTFG (SEQ ID NO: 37), and a variable heavy (V_H) chain comprising a CDRH1 sequence of DYGVS (SEQ ID NO: 38), a CDRH2 sequence of VIWGSETTYYNSALKS (SEQ ID NO: 39), and a CDRH3 sequence of YAMDYWG (SEQ ID NO: 40); or

the scFv comprises a V_L comprising a CDRL1 sequence of FMC63, a CDRL2 sequence of FMC63, a CDRL3 sequence of FMC63, and a V_H comprising a CDRH1 sequence of FMC63, a CDRH2 sequence of FMC63, and a CDRH3 sequence of FMC63; or

(b) the scFv comprises a V_H set forth in SEQ ID NO:41 and a V_L set forth in SEQ ID NO: 42, optionally wherein the V_H and V_L are separated by a flexible linker, optionally wherein the flexible linker is or comprises the sequence set forth in SEQ ID NO:24; and/or (c) wherein the scFv is or comprises the sequence set forth in SEQ ID NO:43.

22. The use of any of claims 1-21, wherein the T cells are primary T cells obtained from a subject; optionally wherein the T cells are autologous to the subject.

23. An article of manufacture comprising a composition of a cell therapy, or one of a plurality of compositions of a cell therapy, comprising T cells expressing an anti-CD19 chimeric antigen receptor (CAR), and instructions for administering the cell therapy, wherein the instructions specify administering the T cell composition according to the use of any of claims 1-22.