IMPROVED FORMULATIONS FOR IMMUNE CELLS

[0001] All documents and online information cited herein are incorporated by reference in their entirety.

REFERENCE TO RELATED APPLICATIONS

[0002] This application claims the benefit of the priority date of U.S. provisional application 62/885,747, filed August 12, 2019, the contents of which are incorporated herein in its entirety.

TECHNICAL FIELD

[0003] The invention is in the field of formulations for immune cells.

BACKGROUND

[0004] T cell activation is an important step in the protective immunity against pathogenic microorganisms *(e.g.,* viruses, bacteria, and parasites), foreign proteins, and harmful chemicals in the environment, and also as immunity against cancer and other hyperproliferative diseases.

[0005] T cells from a donor or a patient can be genetically-modified prior to their administration to the patient. For example, chimeric antigen receptor-expressing T cells may be used in various therapies, including different cancer therapies. Adoptive transfer of T cells expressing chimeric antigen receptors (CARs) is an effective therapy for the treatment of certain hematological malignancies. Modified T cells can also be used after haematopoietic cell transplantation (HCT) and stem cell transplantation (HSCT) to treat and prevent relapse and to provide immunity to the graft patients.

[0006] Genetically modified donor T cells are commonly obtained by taking T cells from the patient or a donor and shipping these to a facility where they are genetically engineered, frozen and returned to the treatment facility where the patient can then receive the therapy. Due to the requirement for the cells to be shipped and frozen, they are usually formulated together with additives such as cryoprotectants to protect the cells.

[0007] Known compositions have sometimes been associated with adverse effects in the recipients or high cost of manufacturing due to some of the additives present in the compositions. There is a need in the art to provide improved formulations which reduce the likelihood of adverse reactions and which can be manufactured in a cost effective manner.

SUMMARY

[0008] The ~~invention~~disclosure meets this need by providing compositions which comprises lower amounts of a cryoprotectant compared to prior art compositions, without any significant loss in cell viability or therapeutic efficacy even at high cell concentrations. These compositions are useful in therapy.

[0008a] In one aspect, the present disclosure provides a composition comprising T cells and serum albumin and dimethyl sulfoxide (DMSO), wherein the composition comprises <2.5% (v/v) serum albumin, and wherein DMSO is present at a >5-fold excess (v/v) compared to the serum albumin. In another aspect, the present disclosure provides a composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.1-1% and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin.

[0008b] In another aspect, the present disclosure provides a composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is 0.1-1% and the concentration of DMSO is 5-7% (v/v); optionally wherein the concentration of serum albumin (v/v) is between 0.2-0.8%, between 0.3-0.7%, between 0.4-0.6%, or about 0.5%. In yet another aspect, the present disclosure provides a composition comprising T cells and serum albumin, wherein (a) the composition comprises about 0.15% (v/v) serum albumin; or (b) the composition also includes dimethyl sulfoxide (DMSO).

[0008c] In a further aspect, the present disclosure provides a composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.03-0.6% and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin; optionally wherein (a) the serum albumin concentration is <0.3% (v/v), and the DMSO concentration is from 8-fold to 11-fold higher than the serum albumin concentration; (b) concentration of DMSO is <3% (v/v); or (c) the concentration of DMSO is from 0.6-2.4% (v/v), from 0.8-2.2% (v/v), from 1.5-2% (v/v), or about 1.8% (v/v). In a further aspect, the present disclosure provides a composition comprising T cells and DMSO, wherein the composition comprises <0.15% (v/v) DMSO. In a further aspect, the present disclosure provides a composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin is 0.03-0.3% (v/v) and the DMSO concentration is 0.15-0.20% (v/v).

[0008d] In a further aspect, the present disclosure provides a process for preparing the composition as described herein, comprising the step of diluting a composition as described herein.

[0008e] In a further aspect, the present disclosure provides a composition as described herein for use in therapy. In a further aspect, the present disclosure provides a use of a composition as described herein in the manufacture of a medicament for treating cancer.

[0008f] In a further aspect, the present disclosure provides a container comprising a suspension of T cells, serum albumin and dimethyl sulfoxide (DMSO), wherein the composition comprises <2.5% (v/v) serum albumin, and wherein DMSO is present at a >5-fold excess (v/v) compared to the serum albumin, and wherein the suspension is to be administered to a patient; optionally wherein (a) the suspension comprises <2.2% (v/v), <2% (v/v), <1% (v/v), or about 0.5% (v/v) serum albumin; and/or (b) DMSO is present at a 5-fold to 30-fold excess (v/v) compared to the

serum albumin; optionally wherein the excess is from 5-fold to 15-fold, from 6-fold to 12-fold, from 8-fold to 11-fold, or about 10-fold.

[0008g] In yet another aspect, the present disclosure provides a container comprising a suspension of T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.1-1% and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin, and wherein the suspension is to be administered to a patient. In yet another aspect, the present disclosure provides a container comprising a suspension of T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is 0.1-1% and the concentration of DMSO is 5-7% (v/v), and wherein the suspension is to be administered to a patient; optionally wherein the concentration of serum albumin (v/v) is between 0.2-0.8%, between 0.3-0.7%, between 0.4-0.6%, or about 0.5%.

[0008h] In yet another aspect, the present disclosure provides a use of a composition as described herein in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered to a patient in need by intravenous infusion; optionally wherein (a) the intravenous infusion time is between 15 and 120 minutes; (b) the intravenous infusion time is up to 30 minutes; (c) the infusion volume is between 50 and 100 mL; or (d) the infusion volume is about 60 mL.

[0008i] In yet another aspect, the present disclosure provides a kit comprising: (a) a container comprising an interior space; and (b) a composition contained within the interior space, wherein the composition comprises: (i) T cells in an amount between about 1 x 10^6 and 40 x 10^6 (e.g., about 5 x 10^6) cells/ml; (ii) serum albumin in a concentration of about 0.1%–0.6% v:v; (iii) DMSO in a concentration of about 5%-7% v:v; and (iv) a pharmaceutically acceptable carrier for human injection; optionally wherein (a) the container comprises a bag, e.g., a cryopreservation bag; optionally wherein the container further comprises a bag spike in fluidic communication with the interior space; (b) the T cells are genetically engineered; (c) the serum albumin is human serum albumin; (d) the serum albumin is present in concentration of about 0.5% v:v; (e) DMSO is present in a concentration of about 5% v:v; (f) the pharmaceutically acceptable carrier comprises sodium chloride, sodium gluconate sodium, acetate trihydrate, potassium chloride, and magnesium chloride; (g) the pharmaceutically acceptable carrier comprises Pharma Lyte; or (h) the composition has a volume of about 15 ml.

[0008j] In yet another aspect, the present disclosure provides a kit comprising: (a) a container comprising an interior space; and (b) a composition contained within the interior space, wherein the composition comprises: (i) T cells in an amount between about 15 x 10^6 cells and about 600 x 10^6 (e.g., about 75 x 10^6) cells; (ii) serum albumin in an amount between about 0.03% and about 1.8% serum albumin, e.g., about 1.5% v:v; (iii) DMSO in a concentration of about 1.5%-2.1 v:v

(e.g., about 1.5% v:v); and (iv) a pharmaceutically acceptable carrier for human injection; optionally wherein (a) the container comprises a bag, optionally including a tube comprising a bag spike, wherein the tube is in fluidic communication with the interior space; or (b) the composition has a volume of about 60 ml.

[0009] We provide a concentrated composition comprising T cells and serum albumin, wherein the composition comprises <2.5% (v/v) serum albumin (preferably <2.2% (v/v), <2% (v/v), or <1% (v/v), and preferably <0.5% (v/v) serum albumin). Such compositions achieve good therapeutic

[0017] In one ~~aspect~~example, the ~~invention~~disclosure provides a container comprising a suspension of T cells, about 5-7% DMSO and about 0.1-1% (*e.g.* 0.2-0.8%, 0.3-0.7%, 0.4-0.6%, or about 0.5%) human albumin (v/v). In some ~~embodiment~~examples, the container is a sterile infusion bag. In some ~~embodiment~~examples, the infusion bag volume is about 15 mL, 30 mL, 50 mL, 60 mL, 70 mL, 100 mL, 250 mL, 500 mL, 750 mL, 1000 mL, 1500 mL, 2000 mL or 3000 mL.

[0018] Concentrated compositions of the ~~invention~~disclosure can be administered to patients, but a high DMSO concentration can sometimes cause cellular damage, so the concentrated compositions can be diluted prior to administration to a patient. This dilution can help to avoid cellular damage. Diluted compositions are ideally administered to patients within 3 hours (*e.g.* within 60-120 minutes, and ideally within 90 minutes) of dilution to avoid even the diluted DMSO from causing cellular damage.

[0019] Thus we also provide a dilute composition comprising T cells and serum albumin, wherein the composition comprises <1% (v/v) serum albumin (preferably <0.6% (v/v), and more preferably 0.15% (v/v)). The dilute composition preferably also includes DMSO at an excess (v/v) compared to the serum albumin of from 3-fold to 30-fold, as described above (*e.g.* at least 5-fold excess DMSO).

[0020] Similarly, we provide a dilute composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.03-0.6% (preferably <0.3% (v/v)) and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin (preferably 3-fold to 15-fold higher *e.g.* from 6-fold to 12-fold higher, from 8-fold to 11-fold higher, or about 10-fold higher).

[0021] The concentration of DMSO in these dilute compositions is preferably <3% (v/v), and is more preferably from 0.6-2.4% (v/v), from 0.8-2.2% (v/v), from 1.5-2% (v/v), or from 1.6-1.9% (v/v), or about 1.77% (v/v).

[0022] We also provide a dilute composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin is 0.03-0.3% (v/v) and the DMSO concentration is 0.15-0.20% (v/v).

[0023] These dilute compositions may comprise between $0.3x10^6$ and $12x10^6$ T cells/mL, for example between $0.3x10^6$ and $10x10^6$ T cells/mL, between $0.3x10^6$ and $12x10^6$ T cells/mL, between $0.3x10^6$ and $9x10^6$ T cells/mL, between $0.3x10^6$ and $7.5x10^6$ T cells/mL, between $0.3x10^6$ and $5x10^6$ T cells/mL, between $0.3x10^6$ and $2x10^6$ T cells/mL, between $0.3x10^6$ and $1.5x10^6$ T cells/mL, or between $0.5x10^6$ and $0.8x10^6$ T cells/mL. A concentration of at least $0.45x10^6$ T cells/mL is typical, and a concentration of about $0.6x10^6$ T cells/mL is preferred.

[0024] Dilute compositions can be (and are intended to be) administered to patients, so they are generally not frozen. Preferably, they will have a temperature of between 4°C and 40°C, for example between 25-40°C, or at body temperature *e.g.* about 37±1°C. Compositions having a temperature between 5°C and 15°C may be typical after removal from a thawing water bath.

[0025] Further provided is a process for preparing a dilute composition as described herein, comprising the step of diluting a concentrated composition as described herein. Dilution may be performed with various liquids *e.g.* with an electrolyte solution (see below). This process may also involve a step of thawing a frozen concentrated composition, followed by the dilution. The diluted composition can then be administered to a patient (*e.g.* without a step of cell culture between dilution and administration).

[0026] The balance of a composition (*i.e.* in addition to the cellular, DMSO and serum albumin components) may be an electrolyte solution (see below). For example, cells may be prepared, then be washed and suspended (and optionally diluted *e.g.* after cryopreservation and thawing) in an electrolyte solution. Thus, a preferred composition may consist essentially of cells, DMSO, serum albumin, and an electrolyte solution.

[0027] The T cells in the concentrated and dilute compositions may be wild-type T cells (*e.g.* polyclonal T cells), but preferably they are genetically modified T cells (*e.g.* CAR-T cells). Genetically-modified T cells may express an activator switch and/or suicide switch. The T cells are most preferably human T cells.

[0028] The serum albumin in the compositions will generally be from the same species as the T cells in the composition. Most preferably, the T cells in the composition are human so, in a most preferred ~~embodiment~~example, the serum albumin is human serum albumin (HSA). This may be prepared from human serum or may be a recombinant human serum albumin.

[0029] Compositions of the ~~invention~~disclosure are suitable and intended for administration to patients during therapy *e.g.* by intravenous infusion. Thus, a composition may be administered to a patient without further cell culture *e.g.* no cell culture medium is added to the composition prior to its administration. The recipient may have a hematological cancer (such as a treatment-refractory hematological cancer) or an inherited blood disorder. For instance, the recipient may have acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), severe combined immune-deficiency (SCID), Wiskott-Aldrich syndrome (WA), Fanconi Anemia, chronic myelogenous leukemia (CML), non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), or multiple myeloma. The composition may help the recipient to control transplant-related infections following receipt of an allograft. The recipient may have received a hematopoietic stem cell transplant (HSCT). The T cells which are administered to a patient will usually be autologous T cells, and will usually have been genetically modified since being removed *e.g.* to express a CAR, a suicide switch, *etc.*

[0030] Thus, we also provide a method of treating a subject, comprising a step of administering a composition as described herein (preferably a dilute composition) to a patient in need thereof. Similarly, we provide the concentrated and dilute compositions, for use in treating a subject. In some ~~embodiment~~examples, the method comprises a step of administering to a patient in need thereof the

compositions described herein by intravenous infusion. In some ~~embodiment~~examples, the intravenous infusion time is between 15 and 120 minutes. In some ~~embodiment~~examples, the intravenous infusion time is up to 30 minutes. In some ~~embodiment~~examples, the infusion volume is between 50 and 100 mL. In some ~~embodiment~~examples, the infusion volume is about 50 mL.

BRIEF DESCRIPTION OF DRAWINGS

[0031] **Figure 1** shows the prediction profiler for post-thaw cell viability.

[0032] **Figure 2** shows the prediction profiler for post-thaw cell recovery.

DETAILED DESCRIPTION

Formulations

[0033] Immune cells, such as T cells (in particular genetically modified T cells), are usually shipped to a patient's location in a frozen state. In order to retain viability during freezing and thawing, the cells are commonly formulated with cryoprotectants to protect them from damage. For example, the cryoprotectant dimethyl sulfoxide (DMSO) is added, usually at a concentration of 10% (v/v), to prevent the formation of ice crystals during the freezing process which could otherwise damage the cells.

[0034] Cryoprotectants such as DMSO have been associated with dose-dependent side effects, such as nausea, vomiting, abdominal cramps, headaches, hypotension, bradycardia, hemolysis, rashes, renal failure, hypertension, heart block, pulmonary edema, cardiac arrest, bronchospasm, and neurologic damage. There have therefore been attempts to reduce the concentration of DMSO to 5% (Morris *et al.* 2014 *Transfusion* 54:2514-22), but compositions still frequently contain 10% DMSO because reducing the concentration is difficult while preserving the cells.

[0035] In order to reduce the potential side effects on a recipient, treatment centers may therefore take measures to reduce the amount of DMSO before infusion, for example through washing the cells. However, this procedure is not ideal because cells can get lost in the process, and each additional handling step inherently increases the chances of contamination.

[0036] Serum albumin is also added to compositions to help in keeping T cells viable during the freeze/thaw cycle. The addition of serum albumin at certain concentrations is deemed essential to preserve the cells during freezing. For example, the formulation for KYMRIAH™ contains 20% (v/v) of 25% human serum albumin (HSA) and YESCARTA™ has 2.5% HSA. Reducing the amount of serum albumin would have the advantage of making the formulations more cost effective but known formulations nonetheless use high concentrations to ensure that the cells are not damaged whilst frozen.

[0037] There is no indication in the prior art that the concentrations of DMSO and serum albumin can both be reduced in these compositions without adversely affecting viability of the T cells.

[0038] The inventors have surprisingly discovered that T cells can be safely formulated using cryoprotectant concentrations which are lower than used in known formulations. These formulations

CLAIMS

1. A composition comprising T cells and serum albumin and dimethyl sulfoxide (DMSO), wherein the composition comprises <2.5% (v/v) serum albumin, and wherein DMSO is present at a ≥5-fold excess (v/v) compared to the serum albumin.

~~2.~~ The composition of claim 1, comprising <2.2% (v/v), <2% (v/v), <1% (v/v), or about 0.5% (v/v) serum albumin; optionally~~.~~

~~3. The composition of claim 1 or claim 2,~~ wherein DMSO is present at a 5-fold to 30-fold excess (v/v) compared to the serum albumin; optionally~~.~~

~~4.~~2.~~The composition of claim 3,~~ wherein the excess is from 5-fold to 15-fold, from 6-fold to 12-fold, from 8-fold to 11-fold, or about 10-fold.

~~5.~~3.A composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.1-1% and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin.

~~6.~~ The composition of claim 3~~5~~, wherein (a) the serum albumin concentration is <1% (v/v), and the DMSO concentration is from 8-fold to 11-fold higher than the serum albumin concentration;~~.~~

~~7. The composition of claim 5~~ or ~~claim 6, wherein~~ (b) concentration of DMSO is <10% (v/v); optionally~~.~~

~~8.~~4.~~The composition of claim 7,~~ wherein the concentration of DMSO is from 2-8% (v/v), from 4-7% (v/v), from 5-6% (v/v), or about 5% (v/v).

~~9.~~ A composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is 0.1-1% and the concentration of DMSO is 5-7% (v/v); optionally~~.~~

~~10.~~5. ~~The composition of claim 9,~~ wherein the concentration of serum albumin (v/v) is between 0.2-0.8%, between 0.3-0.7%, between 0.4-0.6%, or about 0.5%.

~~11.~~6. The composition of any one of claims 1 to ~~10~~5, (a) having between $1x10^6$ and $40x10^6$ T cells/mL and/or (b) wherein the composition is in cryopreserved form.

~~12. The composition of any one of claims 1 to 11, in cryopreserved form.~~

~~13.~~ A composition comprising T cells and serum albumin, wherein (a) the composition comprises about 0.15% (v/v) serum albumin; or (b)~~.~~

~~14.~~7. ~~The~~ the composition ~~of claim 13,~~ also includ~~esing~~ dimethyl sulfoxide (DMSO).

~~15.~~ The composition of claim 7~~14~~, wherein DMSO is present at a 3-fold to 30-fold excess (v/v) compared to the serum albumin; optionally~~.~~

~~16.~~8. ~~The composition of claim 15,~~ wherein the excess is from 3-fold to 15-fold, from 6-fold to 12-fold, from 8-fold to 11-fold, or about 10-fold.

~~17.~~9. A composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.03-0.6% and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin; optionally wherein ~~.~~

~~18.~~ (a)~~The composition of claim 17, wherein~~ the serum albumin concentration is <0.3% (v/v), and the DMSO concentration is from 8-fold to 11-fold higher than the serum albumin concentration; ~~.~~

~~19.~~ (b)~~The composition of claim 17 or claim 18, wherein~~ concentration of DMSO is <3% (v/v); or~~.~~

~~20.~~ (c)~~The composition of claim 7, wherein~~ the concentration of DMSO is from 0.6-2.4% (v/v), from 0.8-2.2% (v/v), from 1.5-2% (v/v), or about 1.8% (v/v).

~~21.~~10. A composition comprising T cells and DMSO, wherein the composition comprises <0.15% (v/v) DMSO.

~~22.~~11. A composition comprising T cells, serum albumin, and DMSO, wherein the concentration of serum albumin is 0.03-0.3% (v/v) and the DMSO concentration is 0.15-0.20% (v/v).

~~23.~~12. The composition of any one of claims 7~~13~~ to 11~~22~~, having between $0.3x10^6$ and $12x10^6$ T cells/mL.

~~24.~~ The composition of any preceding claim, wherein (a) the T cells are genetically modified T cells, such as CAR-T cells; or (b)~~.~~

~~25.~~13. ~~The composition of any preceding claim, wherein~~ the T cells are human T cells and the serum albumin is human serum albumin.

~~26.~~14. A process for preparing the composition of any one of claims 7~~13~~ to 13~~25~~, comprising the step of diluting a composition of any one of claims 1 to 6~~12~~.

~~27.~~ The process of claim 14~~26~~, wherein dilution is performed with an electrolyte solution; optionally~~.~~

~~28. The process of claim 27,~~ wherein (a) the electrolyte solution is normal saline; or (b)~~.~~

29.15. The process of claim 27, wherein the electrolyte solution is a sterile, nonpyrogenic, isotonic solution with a pH of 6.5-8.0 that has about 5.26 g/L NaCl, about 5.02 g/L sodium gluconate, about 3.68 g/L sodium acetate trihydrate, about 0.37 g/L KCl, and about 0.3 g/L $MgCl_2.6H_2O$.

16. A composition of any one of claims 1 to 13 for use in therapy.

30.17. Use of a composition of any one of claims 1 to 13 in the manufacture of a medicament for treating cancerA method of treating a subject, comprising a step of administering a composition of any one of claims 1 to 25 to a patient in need thereof.

31.18. A container comprising a suspension of T cells, serum albumin and dimethyl sulfoxide (DMSO), wherein the composition comprises <2.5% (v/v) serum albumin, and wherein DMSO is present at a ≥5-fold excess (v/v) compared to the serum albumin, and wherein the suspension is to be administered to a patient; optionally wherein .

32. (a)The container of claim 31, wherein the suspension comprises <2.2% (v/v), <2% (v/v), <1% (v/v), or about 0.5% (v/v) serum albumin; and/or.

33. The container of claim 31 orclaim 32, wherein (b) DMSO is present at a 5-fold to 30-fold excess (v/v) compared to the serum albumin; optionally.

34. The container of claim 33, wherein the excess is from 5-fold to 15-fold, from 6-fold to 12-fold, from 8-fold to 11-fold, or about 10-fold.

35.19. A container comprising a suspension of T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is from 0.1-1% and the concentration of DMSO (v/v) is 3-fold to 30-fold higher than the concentration of serum albumin, and wherein the suspension is to be administered to a patient.

36. The container of claim 1935, wherein (a) the serum albumin concentration is <1% (v/v), and the DMSO concentration is from 8-fold to 11-fold higher than the serum albumin concentration; and/or.

37. The container of claim 35 or claim 36, wherein (b) concentration of DMSO is <10% (v/v); optionally).

38.20. The container of claim 37, wherein the concentration of DMSO is from 2-8% (v/v), from 4-7% (v/v), from 5-6% (v/v), or about 5% (v/v).

39. A container comprising a suspension of T cells, serum albumin, and DMSO, wherein the concentration of serum albumin (v/v) is 0.1-1% and the concentration of DMSO is 5-7% (v/v), and wherein the suspension is to be administered to a patient; optionally.

40.21. The container of claim 39, wherein the concentration of serum albumin (v/v) is between 0.2-0.8%, between 0.3-0.7%, between 0.4-0.6%, or about 0.5%.

41.22. The container of any one of claims 1831 to 4021, (a) having between $1x10^6$ and $40x10^6$ T cells/mL; and/or (b) wherein.

42. The the composition of any one of claims 31 to 41, is in cryopreserved form.

43. UseA method of a composition of any one of claims 7 to 13 in the manufacture of a medicament for treating cancer, wherein the medicament is to be administereda subject, comprising a step of administering to a patient in need thereof the composition of any one of claims 13 to 25 by intravenous infusion; optionally.

44. The method of claim 43, wherein (a) the intravenous infusion time is between 15 and 120 minutes; (b) .

45. The method of claim 43, wherein the intravenous infusion time is up to 30 minutes; (c).

46. The method of any one of claims 41-43, wherein the infusion volume is between 50 and 100 mL; or (d).

47.23. The method of any one of claims 1-4, wherein the infusion volume is about 6050 mL.

48.24. The composition, usemethod, process, or container of any preceding claim, wherein the T cells comprise a polynucleotide that encodes a chimeric signaling polypeptide, wherein the chimeric signaling polypeptide comprises:

(i) a costimulatory polypeptide cytoplasmic signaling region;

(ii) a truncated MyD88 polypeptide region lacking the TIR domain;

(iii) a truncated MyD88 polypeptide region lacking the TIR domain and a costimulatory polypeptide cytoplasmic signaling region; or

(iv) a truncated MyD88 polypeptide region lacking the TIR domain and a CD40 cytoplasmic polypeptide region lacking the CD40 extracellular domain;.

49. The composition, method, process, or container of claim 48, optionally wherein costimulatory polypeptide cytoplasmic signaling region is a signaling region that activates the signaling pathways activated by MyD88, CD40 and/or MyD88-CD40 fusion chimeric polypeptide.

~~50.~~25. The composition, use~~method~~, process, or container of any of the preceding claim, wherein the T cells comprises a polynucleotide encoding an inducible chimeric pro-apoptotic polypeptide.

~~51.~~26. A kit comprising:

(a) a container comprising an interior space; and

(b) a composition contained within the interior space, wherein the composition comprises:

(i) T cells in an amount between about 1 x 10^6 and 40 x 10^6 (e.g., about 5 x 10^6) cells/ml;

(ii) serum albumin in a concentration of about 0.1%–0.6% v:v;

(iii) DMSO in a concentration of about 5%-7% v:v; and

(iv) a pharmaceutically acceptable carrier for human injection;~~.~~

~~The kit of claim 51,~~ optionally wherein

~~52.~~ (a) the container comprises a bag, e.g., a cryopreservation bag; optionally~~.~~

~~53.~~ ~~The kit of claim 52,~~ wherein the container further comprises a bag spike in fluidic communication with the interior space.;~~.~~

~~54.~~ (b)~~The kit of claim 51, wherein~~ the T cells are genetically engineered;~~.~~

~~55.~~ (c)~~The kit of claim 51, wherein~~ the serum albumin is human serum albumin;~~.~~

~~56.~~ (d)~~The kit of claim 51, wherein~~ the serum albumin is present in concentration of about 0.5% v:v;~~.~~

~~57.~~ (e)~~The kit of claim 51, wherein~~ DMSO is present in a concentration of about 5% v:v;~~.~~

~~58.~~ (f)~~The kit of claim 51, wherein~~ the pharmaceutically acceptable carrier comprises sodium chloride, sodium gluconate sodium, acetate trihydrate, potassium chloride, and magnesium chloride;

~~59.~~ (g)~~The kit of claim 51, wherein~~ the pharmaceutically acceptable carrier comprises Pharma Lyte; or ~~Plasma Lyte.~~

~~60.~~ (h) ~~The kit of claim 51, wherein~~ the composition has a volume of about 15 ml.

~~61.~~27. A kit comprising:

(a) a container comprising an interior space; and

(b) a composition contained within the interior space, wherein the composition comprises:

(i) T cells in an amount between about 15 x 10^6 cells and about 600 x 10^6 (e.g., about 75 x 10^6) cells;

(ii) serum albumin in an amount between about 0.03% and about 1.8% serum albumin, e.g., about 1.5% v:v;

(iii) DMSO in a concentration of about 1.5%-2.1 v:v (e.g., about 1.5% v:v); and

(iv) a pharmaceutically acceptable carrier for human injection;.

62. The kit of claim 61, optionally wherein (a) the container comprises a bag, optionally including a tube comprising a bag spike, wherein the tube is in fluidic communication with the interior space; or (b) the composition has a volume of about 60 ml.

63. The kit of claim 61, wherein the composition has a volume of about 50 ml.

64. A composition as described herein for use in treating a disease, e.g., cancer.

65. A use of a composition as described herein for treating a disease, e.g., cancer.

66. A use of a composition as described herein in the preparation of a medicament for treating a disease, e.g., cancer.