performing the ACT by administering therapeutic cells to the patient.

[0015a] In one aspect, the present disclosure refers to use of a non-toxic lymphodepleting agent (NTLA) in the manufacture of a medicament for use in a method of enhancing adoptive cellular therapy (ACT) in a human patient with a cancer, autoimmune or infectious disease, wherein the NTLA is dexamethasone or another glucocorticoid, wherein the dexamethasone is to be administered to the patient at a human equivalent dose (HED) of at least 3 mg/kg or another glucocorticoid is to be administered to the patient at an equivalent dose, wherein the method does not include the administration of a chemotherapeutic agent for a duration of 1 day or more; wherein the ACT comprises either a cell used to enhance the immune system in treating the cancer, autoimmune or infectious disease in said patient or a cell derived from an immune lineage which directly treats said cancer, autoimmune or infectious disease.

[0015b] In another aspect, the present disclosure refers to use of a non-toxic lymphodepleting agent (NTLA) in the manufacture of a medicament for use in a method of performing adoptive cellular therapy (ACT) in a human patient with a cancer, autoimmune or infectious disease, wherein the NTLA is dexamethasone or another glucocorticoid formulated to be administered to the patient according to any one of the preceding uses, and the ACT comprises cells used to enhance the immune system in treating the cancer, autoimmune or infectious disease in said patient or cells derived from an immune lineage which directly treats said cancer, autoimmune or infectious disease formulated to be administered to the patient.

[0015c] In some examples, the NTLA is a steroid. The steroid may be a glucocorticoid. In some examples, the steroid is selected from the group consisting of dexamethasone, dexamethasone base, prednisone, methylprednisone, and dexamethasone analogues. In other examples, the NTLA is a selected from the group consisting of tacrolimus and cyclosporine.

[0016] In some examples, the dose of the NTLA achieves at least 60% CD3+ lymphodepletion. Preferably, the dose achieves at least 70%, at least 80% or at least 90% lymphodepletion. In preferred examples, the ACT involves administration of either a cell used to enhance the immune system in treating a disease in said patient or a cell derived from an immune lineage which directly treats said disease.

[0017] In examples in which the NTLA is dexamethasone, the dexamethasone may be administered at a dose of at least about 3 mg/kg, at least about 4 mg/kg, at least about 5 mg/kg, at least about 6 mg/kg, at least about 7 mg/kg, at least about 8 mg/kg, at least about 9 mg/kg, at least about 10 mg/kg, at least about 11 mg/kg, at least about 12 mg/kg, at least about 13 mg/kg, at least about 14 mg/kg, at least about 15 mg/kg, at least about 16 mg/kg, at least about 17 mg/kg, at least about 18 mg/kg, at least about 19 mg/kg, at least about 20 mg/kg, at least about 21 mg/kg, at least about 22 mg/kg, at least about 23 mg/kg, at least about 24 mg/kg, at least about 25 mg/kg, or at least about 26 mg/kg. The NTLA dexamethasone dose may be chosen from a range delimited by dexamethasone dosage values as disclosed herein, e.g. in the present paragraph. For instance the NTLA dexamethasone may be expressed as being administered at a dose chosen from a range of between about 9 mg/kg to about 12 mg/kg. In some examples, the dexamethasone may be administered at a dose of up to about 26 mg/kg.

[0018] Preferably, the NTLA is administered before ACT commences. The NTLA may be administered at least 12 hours before ACT commences. The NTLA may be administered at one or more time points between about 72 to about 12 hours prior to commencement of ACT.

[0019] In a fourth example, this disclosure provides a method of ameliorating the binding and accumulation of a cellular immunotherapy in secondary lymphatic binding sites comprising: identifying a patient suffering from cancer; administering to said patient a cellular immunotherapy comprising either a cell used to enhance the immune system in treating said cancer or a cell derived from an immune lineage which directly treats said cancer; and administering a non-toxic lymphodepleting agent (NTLA), which

Claims

1. Use of a non-toxic lymphodepleting agent (NTLA) in the manufacture of a medicament for use in a method of enhancing adoptive cellular therapy (ACT) in a human patient with a cancer, autoimmune or infectious disease, wherein the NTLA is dexamethasone or another glucocorticoid, wherein the dexamethasone is to be administered to the patient at a human equivalent dose (HED) of at least 3 mg/kg or another glucocorticoid is to be administered to the patient at an equivalent dose, wherein the method does not include the administration of a chemotherapeutic agent for a duration of 1 day or more;

wherein the ACT comprises either a cell used to enhance the immune system in treating the cancer, autoimmune or infectious disease in said patient or a cell derived from an immune lineage which directly treats said cancer, autoimmune or infectious disease.

2. The use according to claim 1, wherein the glucocorticoid is selected from the group consisting of dexamethasone base, prednisone, and methylprednisolone.

3. The use according to claim 2, wherein:

(i) the dexamethasone is to be administered at a human equivalent dose (HED) of at least 4 mg/kg, at least 5 mg/kg, at least 6 mg/kg, at least 7 mg/kg, at least 8 mg/kg, at least 9 mg/kg, at least 10 mg/kg, at least 11 mg/kg, or at least 12 mg/kg;

(ii) the dexamethasone is to be administered at a human equivalent dose (HED) of up to 26 mg/kg; or

(iii) the dexamethasone is to be administered at a human equivalent dose (HED) of between 9 mg/kg to 12 mg/kg.

4. The use according to any of the preceding claims, wherein the enhanced ACT comprises enhanced cancer killing, reduced autoimmune causing cell count, or reduced infectious agent load in a patient with a cancer, autoimmune or infectious disease, respectively.

5. The use according to any of the preceding claims, wherein the NTLA is:

(i) to be administered before ACT commences;

(ii) to be administered at least 12 hours before ACT commences; and / or

(iii) to be administered at one or more time points between 72 to 12 hours prior to commencement of ACT.

6. The use according to any of the preceding claims, wherein the ACT is adoptive T cell therapy.

7. The use according to any of the preceding claims, wherein no radiotherapy and no chemotherapeutic agents are to be administered to the patient.

8. The use according to any of the preceding claims, wherein the patient is a cancer patient and the ACT comprises anticancer T cells and/or anticancer NK cells.

9. Use of a non-toxic lymphodepleting agent (NTLA) in the manufacture of a medicament for use in a method of performing adoptive cellular therapy (ACT) in a human patient with a cancer, autoimmune or infectious disease, wherein the NTLA is dexamethasone or another glucocorticoid formulated to be administered to the patient according to any one of the preceding claims, and the ACT comprises cells used to enhance the immune system in treating the cancer, autoimmune or infectious disease in said patient or cells derived from an immune lineage which directly treats said cancer, autoimmune or infectious disease formulated to be administered to the patient.

10. The use according to any one of the preceding claims, wherein the NTLA induces an elevation of one or more plasma cytokines in the patient, selected from the group consisting of IL-2, IL-7, IL-12, and IL-15 to levels preferably of 20 pg/ml or greater.

11. The use according to any one of the preceding claims, wherein binding and accumulation of the ACT in secondary lymphatic binding sites is ameliorated.