

CLAIMS

What is claimed is:

1. A method of mitigating a non-hematologic severe regimen-related toxicity (SRRT) in a human subject in need thereof, the method comprising intravenously administering a therapeutic composition comprising an effective amount of E4ORF1+ HUVECs to an adult human subject with Hodgkin's lymphoma or non-Hodgkin's lymphoma, wherein: (a) the effective amount is from about 10×10^6 cells per kg bodyweight to about 30×10^6 cells per kg bodyweight, (b) the subject has previously received high-dose therapy (HDT) and an autologous hematopoietic stem cell transplant (AHCT), (c) the E4ORF1+ HUVECs are administered to the subject on the same day that the subject receives the AHCT, and (d) the non-hematologic SRRT is selected from the group consisting of an oral / gastrointestinal SSRT and febrile neutropenia, thereby mitigating the SSRT in the subject.
2. The method of claim 1, wherein the E4ORF1+ HUVECs are administered to the subject from about 2 hours to about 4 hours after the AHCT has been completed.
3. The method of claim 1, wherein the effective amount is from about 10×10^6 cells per kg to about 20×10^6 cells per kg bodyweight.
4. The method of claim 1, wherein the effective amount is about 20×10^6 cells per kg bodyweight.
5. The method of claim 1, further comprising subsequently administering a second dose of the therapeutic composition to the subject.
6. The method of claim 5, wherein the second dose is administered from about 1 day to about 3 days after the AHCT is completed.
7. The method of claim 1, wherein the subject is at least 40 years old.
8. The method of claim 1, wherein the subject is at least 60 years old.

9. The method of claim 1, wherein the therapeutic composition comprises E4ORF1+ HUVECs in a physiological saline.
10. The method of claim 1, wherein the therapeutic composition further comprises one or more excipients selected from the group consisting of buffers, salts, polysaccharides, proteins and preservatives.
11. The method of claim 1, wherein the therapeutic composition further comprises human serum albumin (HSA).
12. The method of claim 1, wherein the therapeutic composition further comprises Dextran40.
13. The method of claim 1, wherein the therapeutic composition further comprises about 0.25% DMSO.
14. The method of claim 1, wherein the therapeutic composition comprises about 5×10^6 E4ORF1+ HUVECs per ml.
15. The method of claim 1, wherein the oral / GI SSRT is selected from the group consisting of mucositis, stomatitis, typhlitis, nausea, vomiting, and diarrhea.
16. The method of claim 15, wherein the mucositis is selected from oral, esophageal, gastric, small intestinal, large intestinal, colonic, rectal or anal mucositis.
17. The method of claim 1, wherein the AHCT comprises transplantation of bone marrow hematopoietic stem cells.
18. The method of claim 1, wherein the AHCT comprises transplantation of peripheral blood hematopoietic stem cells.

19. The method of claim 1, wherein the high dose therapy (HDT) comprises administration to the subject of a combination of chemotherapeutic agents selected from the group consisting of BEAM, BeEAM, FEAM, CBV, TBC, DHAP and Bu/Cy/Flu.
20. The method of claim 1, wherein the method also results in the mitigation of a hematologic SRRT.
21. The method of claim 20, wherein the hematologic SRRT comprises thrombocytopenia, neutropenia, leukopenia, or anemia.
22. The method of claim 20, wherein the time to neutrophil engraftment or platelet engraftment is reduced as compared to the time to neutrophil engraftment or platelet engraftment in a subject not treated with the therapeutic composition.
23. A method of mitigating a non-hematologic severe regimen-related toxicity (SRRT) in a human subject in need thereof, the method comprising: administering a therapeutic composition comprising an effective amount of endothelial cells (ECs) to a human subject who has undergone, is undergoing, or will undergo chemotherapy, wherein the method results in mitigation of a SRRT in the subject.
24. The method of claim 23, wherein the SRRT is selected from the group consisting of an oral/GI toxicity, febrile neutropenia, a solid organ toxicity, veno-occlusive disease, and a severe infection.
25. The method of claim 23, wherein the ECs are human umbilical vein endothelial cells (HUVECs).
26. The method of claim 23, wherein the ECs are E4ORF1+ human umbilical vein endothelial cells (E4ORF1+ HUVECs).
27. The method of claim 23, wherein the subject has a malignant disease.
28. The method of claim 27, wherein the malignant disease is a lymphoma.

29. The method of claim 27, wherein the malignant disease is leukemia.
30. The method of claim 27, wherein the malignant disease is multiple myeloma.
31. The method of claim 27, wherein the malignant disease is myelodysplastic syndrome (MDS).
32. The method of claim 28, wherein the subject has a lymphoma selected from the group consisting of: Hodgkins's lymphoma (HL) and non-Hodgkins's lymphoma (NHL).
33. The method of claim 28, wherein the subject has lymphoma without CNS involvement.
34. The method of claim 28, wherein the subject has lymphoma with CNS involvement (CNS lymphoma).
35. The method of claim 28, wherein the subject has relapsed-refractory lymphoma.
36. The method of claim 23, wherein the chemotherapy is high dose therapy (HDT).
37. The method of claim 23, wherein the chemotherapy is myeloablative chemotherapy.
38. The method of claim 23, wherein the chemotherapy comprises administration to the subject of a combination of chemotherapeutic agents selected from the group consisting of BEAM, BeEAM, FEAM, CBV, TBC, DHAP and Bu/Cy/Flu.
39. The method of claim 23, wherein the chemotherapy is administered to the subject as part of a conditioning regimen to prepare the subject for receipt of a hematopoietic stem cell transplant.
40. The method of claim 23, wherein the subject has received a hematopoietic stem cell transplant.

41. The method of claim 23, wherein the subject has received a hematopoietic stem cell transplant at the time that the therapeutic composition is administered to the subject.
42. The method of claim 23, wherein the subject has received a hematopoietic stem cell transplant within about 3 days of the time that the therapeutic composition is administered to the subject.
43. The method of claim 23, wherein the subject receives a hematopoietic stem cell transplant on the same day that the therapeutic composition is administered to the subject.
44. The method of claim 23, wherein the subject receives a hematopoietic stem cell transplant within about 1 to about 4 hours of the time that the therapeutic composition is administered to the subject.
45. The method of claim 23, wherein the subject receives a hematopoietic stem cell transplant at the same time that the therapeutic composition is administered to the subject.
46. The method of claim 45, wherein the hematopoietic stem cell transplant and the therapeutic composition are administered to the subject in the same IV infusion.
47. The method of any of claims 39-46, wherein the hematopoietic stem cell transplant is an autologous hematopoietic stem cell transplant (ASCT).
48. The method of any of claims 39-46, wherein the hematopoietic stem cell transplant is an allogeneic hematopoietic stem cell transplant (AlloSCT).
49. The method of any of claims 39-48, wherein the subject receives high-dose therapy (HDT) prior to the hematopoietic stem cell transplant.
50. The method of any of claims 23-49, wherein the therapeutic composition comprises ECs at a concentration of about 5 million cells per ml.

51. The method of any of claims 23-50, wherein the therapeutic composition comprises endothelial cells in a physiological saline.
52. The method of any of claims 23-51, wherein the therapeutic composition comprises one or more excipients selected from the group consisting of buffers, salts, polysaccharides, proteins and preservatives.
53. The method of any of claims 23-52, wherein the therapeutic composition comprises human serum albumin (HSA).
54. The method of any of claims 23-53, wherein the therapeutic composition comprises Dextran40.
55. The method of any of claims 23-50, wherein the therapeutic composition comprises DMSO.
56. The method of any of claims 23-55, wherein the therapeutic composition is administered to the subjects intravenously (IV).
57. The method of any of claims 23-56, wherein the therapeutic composition is administered to the subject in single IV infusion.
58. The method of any of claims 23-56, wherein the therapeutic composition is administered to the subject in multiple IV infusions.
59. The method of claim 58, wherein the therapeutic composition is administered to the subject in a first IV infusion on Day 0 and a second IV infusion on Day 1, Day 2, Day 3, Day 4, or Day 5.
60. The method of claim 58, wherein the therapeutic composition is administered to the subject in a first IV infusion on Day 0 and a second IV infusion on Day 3.

61. The method of claim 58, wherein the therapeutic composition is administered to the subject in a first IV infusion on Day 0 and a second IV infusion on Day 2.
62. The method of claim 58, wherein the therapeutic composition is administered to the subject in a first IV infusion on Day 0 and a second IV infusion on Day 1.
63. The method of any of claims 23-62, wherein the effective amount is about 5×10^6 cells per kg bodyweight.
64. The method of claims 23-62, wherein the effective amount is about 10×10^6 cells per kg bodyweight.
65. The method of any of claims 23-62, wherein the effective amount is about 15×10^6 cells per kg bodyweight.
66. The method of any of claims 23-62 wherein the effective amount is about 20×10^6 cells per kg bodyweight.
67. The method of any of claims 23-62, wherein the effective amount is about 25×10^6 cells per kg bodyweight.
68. The method of any of claims 23-62, wherein the effective amount is about 30×10^6 cells per kg bodyweight.
69. The method of any of claims 23-62, wherein the effective amount is about 35×10^6 cells per kg bodyweight.
70. The method of any of claims 23-62, wherein the effective amount is about 40×10^6 cells per kg bodyweight.
71. The method of any of claims 23-62, wherein the effective amount is from about 5×10^6 cells per kg bodyweight to about 40×10^6 cells per kg bodyweight.

72. The method of any of claims 23-62, wherein the effective amount is from about 5×10^6 cells per kg bodyweight to about 25×10^6 cells per kg bodyweight.
73. The method of any of claims 23-62 wherein the effective amount is from about 10×10^6 cells per kg bodyweight to about 20×10^6 cells per kg bodyweight.
74. The method of any of claims 23-62 wherein the effective amount is about 20×10^6 cells per kg bodyweight.
75. The method of any of claims 23-74, wherein the non-hematologic SRRT that is mitigated is selected from the group consisting of mucositis oral, esophageal, gastric, small intestinal, large intestinal, colonic, rectal or anal mucositis), stomatitis, typhlitis, nausea, vomiting, and diarrhea.
76. The method of any of claims 23-75, wherein the method also results in the mitigation of a hematologic SRRT.
77. The method of claim 76, wherein the hematologic SRRT comprises thrombocytopenia, neutropenia, leukopenia, or anemia.
78. The method of claim 76, wherein the time to neutrophil engraftment or platelet engraftment is reduced as compared to the time to neutrophil engraftment or platelet engraftment in a subject not treated with the therapeutic composition.
79. The method of any of claims 23-79, wherein the ECs are E4ORF1+ ECs.
80. The method of any of claims 23-78, wherein the ECs are E4ORF1+ HUVECs
81. A method of mitigating a chemotherapy side effect in a human subject in need thereof, the method comprising: administering a therapeutic composition comprising an effective amount of endothelial cells (ECs) to a human subject who has undergone, is undergoing, or will undergo chemotherapy, wherein the method results in mitigation of the chemotherapy side effect in the subject.

82. The method of claim 81, wherein the ECs are E4ORF1+ ECs.
83. The method of claim 81, wherein the ECs are E4ORF1+ HUVECs