

We Claim:

1. A method for determining a risk of an adverse event upon administration of an immunotherapy to a cancer subject in need thereof, the method comprising:

quantifying a baseline serum level from the cancer subject of REG3A; or

quantifying a day 0 serum level from the cancer subject of REG3A; and

wherein at least one of an increased baseline serum level of REG3A versus a control baseline serum level of REG3A and/or an increased day 0 serum level of REG3A versus a control day 0 serum level of REG3A indicates an increased risk of the adverse event in the cancer subject,

wherein the adverse event is one or more of a Grade 3+ CRS, and a Grade 3+ NE.

2. The method of claim 1, wherein the method comprises

quantifying a baseline serum level from the cancer subject of REG3A; and

quantifying a day 0 serum level from the cancer subject of REG3A.

3. The method of claim 1 or 2, wherein the method comprises quantifying a baseline serum level from the cancer subject of REG3A and one or more biomarkers selected from KYN, OSMR, NELL2, and MET.

4. The method of any one of claims 1-3, wherein the method comprises quantifying a day 0 serum level from the cancer subject of REG3A and one or more biomarkers selected from SOD2, VAMP5, PCDH17, ACE2, REG1B, AREG, CELA3A, CEACAM1, STK11, LY9, LY96, CKAP4, CXCL1, EIF5A, IL1A, KIFBP, KIRREL2, NUB1, PAG1, PCDH17, TGFB1, ADAM15, BSG, HLA-DRA, ICAM2, OSMR, SERPINB9, CCL16, MEGF9, and MFAP5.

5. The method of any one of claims 1-4, wherein the control baseline serum level of REG3A is a historically observed baseline serum level of REG3A not previously observed to be associated with an onset of the adverse event, and wherein the control day 0 serum level of REG3A is a historically observed day 0 serum level of REG3A not previously observed to be associated an onset of the adverse event.

6. The method of any one of claims 1-5, wherein it is indicated that the cancer subject has an increased risk of the adverse event if the baseline serum level of REG3A and the day 0 serum level of REG3A is above a predetermined normalized protein expression range for REG3A, wherein the predetermined normalized protein expression range is 1.80-2.19 for REG3A (baseline), and 2.34-2.88 for REG3A (day 0).

7. The method of any one of claims 1-6, wherein the increased risk of an adverse event in the cancer subject indicates one or more of the following: the cancer subject should be treated with a modified pre-conditioning regimen versus a standard pre-conditioning regimen, the cancer subject should not be administered the immunotherapy, the cancer subject should be administered the immunotherapy with a modified dose versus a standard dose, or the cancer subject should be administered the immunotherapy in combination with an agent for reducing a Grade 3+ CRS, and/or a Grade 3+ NE.

8. The method of claim 7, wherein the modified pre-conditioning regimen comprises administering to the cancer subject a modified dose of at least one of cyclophosphamide and fludarabine instead of a predetermined dose of cyclophosphamide or fludarabine administered to a control subject.

9. The method of any of claims 1-8, , wherein the increased risk of an adverse event in the cancer subject indicates that the cancer subject should be administered the immunotherapy with a combination therapy comprising an agent that reduces cytokine induction and/or endothelial cells disruption.

10. The method of claim 9, wherein the agent reduces cytokine induction.

11. The method of claim 10, wherein the agent is administered to the cancer subject prior to administration of the immunotherapy, before a peak expansion of the immunotherapy, or at the peak expansion of the immunotherapy.

12. The method of any one of claims 9-11, wherein the agent is selected from an anti-IL-1 molecule, a T-cell activation inhibitor, a JAK inhibitor, an anti-GM-CSF molecule, an anti-TNF molecule, an Ang2 inhibitor, an anti-angiogenic therapy, and an anti-IFN γ molecule.

13. The method of any one of claims 1-12, wherein the immunotherapy is a CAR T cell therapy, a TCR T cell therapy, a tumor infiltrating lymphocytes (TIL) cell therapy, or a bispecific T-cell engagers (BiTEs) therapy.

14. The method of claim 13, wherein the immunotherapy is autologous or allogeneic.

15. The method of claim 13, wherein the immunotherapy is CAR T or TCR T cell therapy that recognizes a target antigen.

16. The method of claim 15, wherein the target antigen is a tumor antigen selected from a tumor associated surface antigen, lineage-specific or tissue specific antigen, virus-specific surface antigen, and GPC3 (Glypican 3), as well as any derivate or variant of these antigens.

17. The method of any one of claims 1-16, wherein the cancer subject has a cancer or tumor selected from a solid tumor, sarcoma, carcinoma, lymphoma, multiple myeloma, Hodgkin's Disease, non-Hodgkin's lymphoma (NHL), primary mediastinal large B cell lymphoma (PMBCL), diffuse large B cell lymphoma (DLBCL) (not otherwise specified), follicular lymphoma (FL), DLBCL arising from FL, transformed follicular lymphoma, high grade B cell lymphoma, splenic marginal zone lymphoma (SMZL), chronic or acute leukemia, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia (ALL) (including non T cell ALL), chronic lymphocytic leukemia (CLL), T-cell lymphoma, one or more of B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL), chronic myelogenous leukemia (CML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, myelodysplasia and myelodysplastic syndrome, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, a plasma cell

proliferative disorder, monoclonal gammopathy of undetermined significance (MGUS), plasmacytomas, systemic amyloid light chain amyloidosis, POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome), head and neck cancers, cervical cancers, ovarian cancers, non-small cell lung carcinomas, hepatocellular carcinomas, prostate cancers, breast cancers, or a combination thereof.

18. The method of claim 17, wherein the cancer is (relapsed or refractory) diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, DLBCL arising from follicular lymphoma, or mantle cell lymphoma.

19. The method of any one of claims 1-18, wherein the immunotherapy is selected from axicabtagene ciloleucel, brexucabtagene autoleucel, tisagenlecleucel, lisocabtagene maraleucel, and bb2121.