[11] Immunoregulatory modulating agents include (i) an agent that blockades CD47 activity; and (ii) one or more of an agent that agonizes an immune costimulatory molecule, e.g. CD40, OX40, etc.; and/or (iii) an agent that antagonizes an immune inhibitory molecule, e.g. CTLA-4, PD1, PDL1, *etc*. The active agents are administered within a period of time to produce an additive or synergistic effect on depletion of cancer cells in the host. Administration may be Methods of administration include, without limitation, systemic administration, intra-tumoral administration, etc. Usually the active agent (i) is administered within about a period of about 45 days, about 30 days, about 21 days, about 14 days, about 10 days, about 8 days, about 7 days, about 6 days, about 5 days, about 4 days, about 3 days, about 2 days, about 1 day or substantially the same day as an agent (ii) and/or (iii). In some examples an agent (i) is administered prior to an agent (ii) and/or (iii). In some examples an agent (i) is administered after an agent (ii) and/or (iii). The agents can be considered to be combined if administration scheduling is such that the serum level of both agents is at a therapeutic level at the same time. Administration may be repeated as necessary for depletion of the cancer cell population.

[11a] In one aspect, the present disclosure refers to a use of a combination of (i) an antibody that blockades CD47 activity; and (ii) an antibody that antagonizes CTLA4, in the manufacture of a medicament for targeting cancer cells for immunodepletion in a human, wherein the antibody that blockades CD47 activity is to be administered with antibody (ii); and

wherein a population of cells comprising the targeted cells is to be contacted with the medicament, and wherein said combination is in a dose effective to increase depletion of the targeted cells, and wherein the contacting is to be performed in a human subject; and wherein the combination of antibodies provides a synergistic effect relative to the administration of the anti-CTLA4 antibody or the anti-CD47 antibody as a monotherapy.

[12] In some examples, an individual cancer is selected for treatment with a combination therapy of the present disclosure because the cancer is a cancer type that is responsive to a checkpoint inhibitor, e.g. a PD1 antagonist, a PDL1 antagonist, a CTLA4 antagonist, a TIM-3 antagonist, a BTLA antagonist, a VISTA antagonist, a LAG3 antagonist; etc. In some examples, such an immunoregulatory agent is a CTLA-4, PD1 or PDL1 antagonist, e.g. avelumab, nivolumab, pembrolizumab, ipilimumab, and the like. In some such examples the cancer is, without limitation, melanoma or small cell lung cancer. In some such examples, the cancer is a type that has a high neoantigen, or mutagenesis, burden (see Vogelstein et al. (2013) Science 339(6127):1546-1558, herein specifically incorporated by reference). In other examples, the cancer with a type with a low neoantigen burden. In some such examples, the combination therapy of the present disclosure enhances the activity of the checkpoint inhibitor. In other examples, where the individual cancer does not respond to a checkpoint inhibitor alone, the combination therapy provides a therapeutic response.

What is Claimed is:

1. Use of a combination of (i) an antibody that blockades CD47 activity; and (ii) an antibody that antagonizes CTLA4, in the manufacture of a medicament for targeting cancer cells for immunodepletion in a human, wherein the antibody that blockades CD47 activity is to be administered with antibody (ii); and

wherein a population of cells comprising the targeted cells is to be contacted with the medicament, and wherein said combination is in a dose effective to increase depletion of the targeted cells, and wherein the contacting is to be performed in a human subject; and wherein the combination of antibodies provides a synergistic effect relative to the administration of the anti-CTLA4 antibody or the anti-CD47 antibody as a monotherapy.

2. The use of any one of claim 1, wherein the combination further comprises an antibody that binds to an antigen on the targeted tumor cell.

3. The use of claim 1, wherein the treatment provides for increased overall survival of the individual.

4. The use of any of claims 1-3, wherein the antibody that blockades CD47 activity is an anti-CD47 antibody.

5. The use of claim 4, wherein the anti-CD47 antibody comprises an IgG4 Fc region.

6. The use of claim 5 wherein the antibody is 5F9-G4.

7. The use of claim 4, wherein a priming dose of the antibody that blockades CD47 activity is to be further administered.

8. The use of claim 4, wherein a priming dose of an erythropoietin stimulating agent is to be further administered.

9. The use of any one of claims 1-8, wherein the cancer cells are solid tumor cells, optionally wherein the cancer cells are carcinoma, sarcoma, glioblastoma, melanoma, lymphoma, or myeloma cells.

10. The use of claim 9, wherein the cancer cells are ovarian cancer cells.

11. The use of any one of claims 1-10, wherein the antagonistic anti-CTLA4 antibody is ipilimumab.