

SUMMARY

[0005a] In one aspect of the present disclosure, there is provided a use of a combination of:

(i) an agent that selectively blocks CD47 binding to SIRP α , selected from: an antibody that binds to CD47; an antibody that binds to SIRP α ; and a soluble high affinity SIRP α polypeptide or a combination thereof; and

(ii) an antibody that specifically binds to one or more cell-surface antigens on lung cancer cells wherein the one or more cell-surface antigens on lung cancer cells are selected from CD99, CD44 and EpCAM,

in the manufacture of a medicament for treating an individual with small cell lung cancer (SCLC), wherein the medicament is to be administered in a dose effective to increase depletion of the SCLC cells.

[0006] Methods and compositions are also provided for the treatment of lung cancer with a targeted therapy. In some embodiments, the lung cancer is small cell lung cancer. In some embodiments, the therapy is targeted at one or more cell-surface antigens, including CD24, CD166, CD56, CD326, CD298, CD29, CD63, CD9, CD164, CD99, CD46, CD59, CD57, CD165, EpCAM, *etc.* In some embodiments the targeted therapy comprises administering to an individual suffering from lung cancer a therapeutic dose of an antibody that specifically binds to a cell surface marker selected from CD24, CD166, CD56, CD326, CD298, CD29, CD63, CD9, CD164, CD99, CD46, CD59, CD57, CD165 and EpCAM.

[0007] In some embodiments the targeted therapy is combined with a CD47 blocking agent. Cancer cells evade macrophage surveillance by upregulation of CD47 expression. Administration of agents that mask the CD47 protein, *e.g.* antibodies or small molecules that bind to CD47 or SIRP α and prevent interaction between CD47 and SIRP α , are administered to a patient, which increases the clearance of cancer cells via phagocytosis. The agent that blocks CD47 is combined with monoclonal antibodies directed against one or more lung cancer cell markers, which compositions can be synergistic in enhancing phagocytosis and elimination of cancer cells as compared to the use of single agents.

[0008] Specific reagent combinations of interest for therapy include anti-CD47 and anti-CD56; anti-CD47 and anti-CD44, anti-CD47 and anti-CD99, anti-CD47 and anti-EpCAM. In some such embodiments the anti-CD47 reagent is a high affinity SIRP α polypeptide, which can be provided in the form of a monomer or a multimer, *e.g.* as a fusion protein with an IgG Fc polypeptide.

[0009] In other embodiments, the therapy provides for a multispecific antibody that targets CD47 and a second cancer cell marker, including multispecific antibodies that target CD47 and CD56; CD47 and CD44, CD47 and EpCAM, *etc.* Compositions of such multispecific antibodies are also provided, where the multispecific antibody is desirably

WHAT IS CLAIMED IS:

1. Use of a combination of:
 - (i) an agent that selectively blocks CD47 binding to SIRP α , selected from: an antibody that binds to CD47; and antibody that binds to SIRP α ; and a soluble high affinity SIRP α polypeptide or a combination thereof; and
 - (ii) an antibody that specifically binds to one or more cell-surface antigens on lung cancer cells wherein the one or more cell-surface antigens on lung cancer cells are selected from CD99, CD44 and EpCAM,in the manufacture of a medicament for treating an individual with small cell lung cancer (SCLC), wherein the medicament is to be administered in a dose effective to increase depletion of the SCLC cells.
2. The use of claim 1, wherein the agent that selectively blocks CD47 binding to SIRP α is an antibody.
3. The use of claim 2, wherein the antibody specifically binds to CD47.
4. The use of claim 2, wherein the antibody specifically binds to SIRP α .
5. The use of claim 1, wherein the agent that selectively blocks CD47 binding to SIRP α is a soluble SIRP α polypeptide.
6. The use of claim 1, wherein the combination of agents is to be administered simultaneously.
7. The use of claim 1, wherein the combination of agents is to be administered sequentially.
8. The use of claim 1, wherein the combination of agents is to be administered in overlapping dosing regimens.
9. The use of claim 1, wherein the individual is a human.

10. The use of claim 1, wherein the combination of agents provides for a synergistic effect.

11. The use of claim 3 wherein the antibody is 5F9-G4.