

immunocytokines or FAP-targeted IL-2 variant immunocytokines, respectively, described herein.

In one aspect, there is provided a tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use as a combination therapy in the treatment of cancer,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or

c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or

d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126,

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or

b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or

c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or

d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or

e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or

f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or

g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or

h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or

i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or

- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided a CEA-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use in

- i) inhibition of tumor growth in a CEA-expressing tumors; and/or
- ii) enhancing median and/or overall survival of subjects with a CEA-expressing tumor,

wherein the CEA-targeted IL-2 variant immunocytokine is administered in combination with an antibody which binds to human PD-L1;

wherein the CEA-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- m) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:104, or
- n) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:105, or
- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided a FAP-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use in

- i) inhibition of tumor growth in a FAP-expressing tumor; and/or
- ii) enhancing median and/or overall survival of subjects with a FAP-expressing tumor;

wherein the FAP-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- b) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

- l) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:103, or
- m) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:104, or
- n) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:105, or
- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided a tumor-targeted IL-2 variant immunocytokine, for use in the treatment of a patient having a CEA-expressing tumor or a tumor characterized by expression or overexpression of CEA, having a FAP-expressing tumor or a tumor characterized by expression or overexpression of FAP or having a tumor associated with expression or overexpression of CEA or FAP, and wherein the immunocytokine is administered in combination with an antibody which binds to human PD-L1,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or

In another aspect, there is provided use of a tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament as a combination therapy in the treatment of cancer,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126,

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided use of a tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament for the

- i) inhibition of tumor growth in a tumor expressing the target of the immunocytokine; and/or
- ii) enhancing median and/or overall survival of subjects with a tumor expressing the target of the immunocytokine;

wherein the target is presented on a tumor cell or in a tumor cell environment,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or

- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or
- f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or
- g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or
- h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or
- i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or
- j) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:101, or

- k) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:102, or
- l) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:103, or
- m) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:104, or
- n) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:105, or
- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided use of a CEA-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament for the

- i) inhibition of tumor growth in a CEA-expressing tumors; and/or
- ii) enhancing median and/or overall survival of subjects with a CEA-expressing tumor,

wherein the CEA-targeted IL-2 variant immunocytokine is administered in combination with an antibody which binds to human PD-L1;

wherein the CEA-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or
- f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or
- g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or
- h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or
- i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or
- j) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:101, or
- k) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:102, or

- l) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:103, or
- m) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:104, or
- n) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:105, or
- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided use of a FAP-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament for the

- i) inhibition of tumor growth in a FAP-expressing tumor; and/or
- ii) enhancing median and/or overall survival of subjects with a FAP-expressing tumor;

wherein the FAP-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- b) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

In another aspect, there is provided use of a tumor-targeted IL-2 variant immunocytokine in the manufacture of a medicament for the treatment of a patient having a CEA-expressing tumor or a tumor characterized by expression or overexpression of CEA, having a FAP-expressing tumor or a tumor characterized by expression or overexpression of FAP or having a tumor associated with expression or overexpression of CEA or FAP, and wherein the immunocytokine is to be administered in combination with an antibody which binds to human PD-L1,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or

- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or
- f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or
- g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or
- h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or
- i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or
- j) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:101, or
- k) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:102, or

Claims

1. A tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use as a combination therapy in the treatment of cancer,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or

c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or

d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126,

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or
- f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or
- g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or
- h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or
- i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or

4. The tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 according to claim 1, for use in the prevention or treatment of metastasis.
5. The tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 according to claim 1, for use in the treatment of inflammatory diseases.
6. The tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 according to claim 1, for use in treating or delaying progression of an immune related disease such as tumor immunity.
7. The tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 according to claim 1 for use in stimulating an immune response or function, such as T cell activity.
8. A tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use in
 - i) inhibition of tumor growth in a tumor expressing the target of the immunocytokine; and/or
 - ii) enhancing median and/or overall survival of subjects with a tumor expressing the target of the immunocytokine;wherein the target is presented on a tumor cell or in a tumor cell environment,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or

p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

9. A CEA-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use in

- i) inhibition of tumor growth in a CEA-expressing tumors; and/or
- ii) enhancing median and/or overall survival of subjects with a CEA-expressing tumor;

wherein the CEA-targeted IL-2 variant immunocytokine is administered in combination with an antibody which binds to human PD-L1;

wherein the CEA-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- m) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:104, or
 - n) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:105, or
 - o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
 - p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.
10. A FAP-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 for use in
- i) inhibition of tumor growth in a FAP-expressing tumor; and/or
 - ii) enhancing median and/or overall survival of subjects with a FAP-expressing tumor;
- wherein the FAP-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising
- a) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
 - b) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

- l) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:103, or
 - m) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:104, or
 - n) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:105, or
 - o) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:106, or
 - p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.
11. A tumor-targeted IL-2 variant immunocytokine, for use in the treatment of a patient having a CEA-expressing tumor or a tumor characterized by expression or overexpression of CEA, having a FAP-expressing tumor or a tumor characterized by expression or overexpression of FAP or having a tumor associated with expression or overexpression of CEA or FAP, and wherein the immunocytokine is administered in combination with an antibody which binds to human PD-L1,
- wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising
- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or

- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or

16. The tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 according to any one of the preceding claims, wherein the effectorless Fc mutation is L234A/L235A or L234A/L235A/P329G or N297A or D265A/N297A.
17. Use of a tumor-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament as a combination therapy in the treatment of cancer,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising
 - a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
 - b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or

- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126,

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or
- f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or
- g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or
- h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or
- i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or

19. Use of a CEA-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament for the

- i) inhibition of tumor growth in a CEA-expressing tumors; and/or
- ii) enhancing median and/or overall survival of subjects with a CEA-expressing tumor,

wherein the CEA-targeted IL-2 variant immunocytokine is administered in combination with an antibody which binds to human PD-L1;

wherein the CEA-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or

- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

20. Use of a FAP-targeted IL-2 variant immunocytokine in combination with an antibody which binds to human PD-L1 in the manufacture of a medicament for the

- i) inhibition of tumor growth in a FAP-expressing tumor; and/or
- ii) enhancing median and/or overall survival of subjects with a FAP-expressing tumor;

wherein the FAP-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or
- b) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or

- p) a heavy chain variable domain VH of SEQ ID NO:91 and a light chain variable domain VL of SEQ ID NO:107.

21. Use of a tumor-targeted IL-2 variant immunocytokine in the manufacture of a medicament for the treatment of a patient having a CEA-expressing tumor or a tumor characterized by expression or overexpression of CEA, having a FAP-expressing tumor or a tumor characterized by expression or overexpression of FAP or having a tumor associated with expression or overexpression of CEA or FAP, and wherein the immunocytokine is to be administered in combination with an antibody which binds to human PD-L1,

wherein the tumor-targeted IL-2 variant immunocytokine used in the combination therapy is characterized in comprising

- a) the polypeptide sequences of SEQ ID NO:84, and SEQ ID NO:86 and SEQ ID NO:88, or
- b) the polypeptide sequences of SEQ ID NO:108, and SEQ ID NO:109 and SEQ ID NO:110, or
- c) the polypeptide sequences of SEQ ID NO:79, and SEQ ID NO:80 and SEQ ID NO:81, or

- d) the polypeptide sequences of SEQ ID NO:124, and SEQ ID NO:125 and SEQ ID NO:126;

and the antibody which binds to human PD-L1 used in the combination therapy is characterized in comprising

- a) a heavy chain variable domain VH of SEQ ID NO:89 and a light chain variable domain VL of SEQ ID NO:92, or
- b) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:93, or
- c) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:94, or
- d) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:95, or
- e) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:96, or
- f) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:97, or
- g) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:98, or
- h) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:99, or
- i) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:100, or
- j) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:101, or
- k) a heavy chain variable domain VH of SEQ ID NO:90 and a light chain variable domain VL of SEQ ID NO:102, or