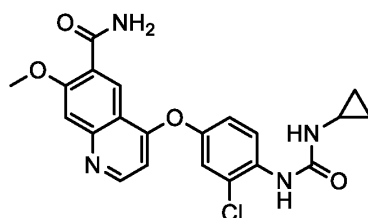


Claims

1. A pharmaceutical combination comprising a substance A and a substance B;
wherein the substance A is Compound F, a crystal form thereof, a pharmaceutically acceptable salt thereof or a solvate thereof;



Compound F

the substance B is an antibody M comprising a heavy chain CDR amino acid sequence selected from the group consisting of: SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21 and 23, or an antigen binding fragment thereof.

2. The pharmaceutical combination as defined in claim 1, wherein the antibody M comprises:

(a) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 1, a HCDR2 amino acid sequence of SEQ ID NO: 3, and a HCDR3 amino acid sequence of SEQ ID NO: 5; and a light chain variable region comprising a LCDR1 amino acid sequence of SEQ ID NO: 2, a LCDR2 amino acid sequence of SEQ ID NO: 4, and a LCDR3 amino acid sequence of SEQ ID NO: 6;

(b) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 7, a HCDR2 amino acid sequence of SEQ ID NO: 9, and a HCDR3 amino acid sequence of SEQ ID NO: 11; and a light chain variable region comprising a LCDR1 amino acid sequence of SEQ ID NO: 8, a LCDR2 amino acid sequence of SEQ ID NO: 10, and a LCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 13, a HCDR2 amino acid sequence of SEQ ID NO: 15, and a HCDR3 amino acid sequence of SEQ ID NO: 17; and a light chain variable region comprising a LCDR1 amino acid sequence of SEQ ID NO: 14, a LCDR2 amino acid sequence of SEQ ID NO: 16, and a LCDR3 amino acid sequence of SEQ ID NO: 18; or

(d) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 19, a HCDR2 amino acid sequence of SEQ ID NO: 21, and a HCDR3 amino acid sequence of SEQ ID NO: 23; and a light chain variable region comprising a LCDR1 amino acid sequence of SEQ ID NO: 8, a LCDR2 amino acid sequence of SEQ ID NO: 10, and a LCDR3 amino acid

sequence of SEQ ID NO: 12;

optionally, the antibody M comprises a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 7, a HCDR2 amino acid sequence of SEQ ID NO: 9, and a HCDR3 amino acid sequence of SEQ ID NO: 11; and a light chain variable region comprising a LCDR1 amino acid sequence of SEQ ID NO: 8, a LCDR2 amino acid sequence of SEQ ID NO: 10, and a LCDR3 amino acid sequence of SEQ ID NO: 12.

3. The pharmaceutical combination as defined in claim 1 or 2, wherein the antibody M comprises:

(a) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 20; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 22;

(b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 24; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 25;

(c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 26; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 27; or

(d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 28; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 25;

optionally, the antibody M comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 24; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 25.

4. The pharmaceutical combination as defined in any one of claims 1-3, wherein the antibody M comprises a heavy chain constant region of human IgG4, and a light chain constant region of human λ or κ light chain;

and/or, the substance B is the antibody M;

and/or, the substance A is the mesylate of Compound F;

and/or, the pharmaceutical combination further comprises a pharmaceutical excipient.

5. The pharmaceutical combination as defined in any one of claims 1-4, wherein the pharmaceutical combination is in the form of a fixed combination or a non-fixed combination, optionally, in the form of a non-fixed combination.

6. A pharmaceutical composition comprising a substance A and a substance B; wherein the substance A and the substance B are as defined in any one of claims 1-4.

7. A kit comprising:

a first container comprising a first pharmaceutical composition comprising a substance A;

and

a second container comprising a second pharmaceutical composition comprising a

substance B;

wherein the substance A and the substance B are as defined in any one of claims 1-4.

8. A method for treating a cancer comprising administering the pharmaceutical combination as defined in any one of claims 1-5 or the pharmaceutical composition as defined in claim 6.

9. The method as defined in claim 8, wherein the cancer is non-small cell lung cancer, small cell lung cancer, renal cell cancer, colorectal cancer, colon cancer, ovarian cancer, breast cancer, pancreatic cancer, gastric carcinoma, bladder cancer, esophageal cancer, mesothelioma, melanoma, head and neck cancer, thyroid cancer, sarcoma, prostate cancer, glioblastoma, cervical cancer, thymic carcinoma, leukemia, lymphomas or myelomas; optionally, the cancer is colon cancer;

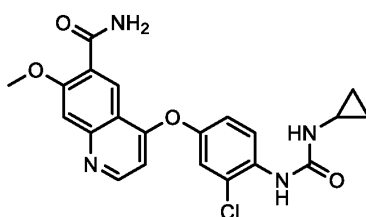
and/or, the substance A and the substance B are administrated simultaneously or separately, optionally, administrated separately;

and/or, the substance A is administrated orally;

and/or, the substance B is administrated by injection.

10. A pharmaceutical combination comprising a substance A and a substance C;

wherein the substance A is Compound F, a crystal form thereof, a pharmaceutically acceptable salt thereof or a solvate thereof;



Compound F

the substance C is an antibody N comprising a CDR amino acid sequence selected from the group consisting of SEQ ID NOs: 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50 and 51, or an antigen binding fragment thereof.

11. The pharmaceutical combination as defined in claim 10, wherein the antibody N comprises:

(a) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence selected from the group consisting of SEQ ID NOs: 40 and 41; and

(b) a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 43, 44, 45 and 46, a LCDR2 amino acid sequence of

SEQ ID NO: 47, and a LCDR3 amino acid sequence selected from the group consisting of SEQ ID NOs: 48, 49, 50 and 51.

12. The pharmaceutical combination as defined in claim 10 or 11, wherein the antibody N comprises:

(a) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 40; and a light chain variable region comprising a LCDR1 amino acid sequence of SEQ ID NO: 42, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 48;

(b) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 41; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 42, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49;

(c) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 41; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 43, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49;

(d) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 41; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 44, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49;

(e) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 40; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 45, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49;

(f) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 40; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 44, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49;

(g) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence

of SEQ ID NO: 41; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 45, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49;

(h) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 41; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 45, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 50;

(i) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 40; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 46, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 51; or

(j) a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 40; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 46, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 48;

optionally, the antibody N comprises a heavy chain variable region comprising a HCDR1 amino acid sequence of SEQ ID NO: 38, a HCDR2 amino acid sequence of SEQ ID NO: 39, and a HCDR3 amino acid sequence of SEQ ID NO: 41; and a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of SEQ ID NO: 42, a LCDR2 amino acid sequence of SEQ ID NO: 47, and a LCDR3 amino acid sequence of SEQ ID NO: 49.

13. The pharmaceutical combination as defined in any one of claims 10-12, wherein the antibody N comprises:

(a) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 31;

(b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 31;

(c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 32;

(d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 33;

(e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 34;

(f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29;

and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 33;

(g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 34;

(h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 35;

(i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 36; or

(j) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 37;

optionally, the antibody N comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 30; and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 31.

14. The pharmaceutical combination as defined in any one of claims 10-13, wherein the antibody N further comprises a heavy chain constant region of human IgG4, and a light chain constant region of human λ or κ light chain;

and/or, the substance C is the antibody N;

and/or, the substance A is the mesylate of Compound F;

and/or, the pharmaceutical combination further comprises a pharmaceutical excipient.

15. The pharmaceutical combination as defined in any one of claims 10-14, wherein the pharmaceutical combination is in the form of a fixed combination or a non-fixed combination, optionally, in the form of a non-fixed combination.

16. A pharmaceutical composition comprising a substance A and a substance C; wherein the substance A and the substance C are as defined in any one of claims 10-14.

17. A kit comprising:

a first container comprising a first pharmaceutical composition comprising a substance A; and

a second container comprising a second pharmaceutical composition comprising a substance C;

wherein the substance A and the substance C are as defined in any one of claims 10-14.

18. A method for treating a cancer comprising administering the pharmaceutical combination as defined in any one of claims 10-15 or the pharmaceutical composition as defined in claim 16.

19. The method as defined in claim 18, wherein the cancer is non-small cell lung cancer,

small cell lung cancer, renal cell cancer, colorectal cancer, colon cancer, ovarian cancer, breast cancer, pancreatic cancer, gastric carcinoma, bladder cancer, esophageal cancer, mesothelioma, melanoma, head and neck cancer, thyroid cancer, sarcoma, prostate cancer, glioblastoma, cervical cancer, thymic carcinoma, leukemia, lymphomas or myelomas; optionally, the cancer is colon cancer;

and/or, the substance A and the substance C are administrated simultaneously or separately, optionally, administrated separately;

and/or, the substance A is administrated orally;

and/or, the substance C is administrated by injection.