

SUMMARY

The disclosure provides alternative, convenient, cost efficient, subcutaneous dosing regimens for treating a cancer patient with an anti-PD-1 antibody, or antigen-binding fragment thereof, wherein the dosing schedule is expected to provide a safe and effective dose of the anti-PD-1 antibody, or antigen-binding fragment thereof. Specifically, the disclosure provides a method of treating cancer in a human patient comprising subcutaneously administering about 280 mg to about 450 mg of an anti-PD-1 antibody, or antigen binding fragment thereof, to the patient every three weeks; wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises (a) light chain (LC) complementarity determining regions (CDRs) LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 1, 2 and 3, respectively, and heavy chain (HC) CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 6, 7 and 8, respectively; or (b) light chain CDRs LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 11, 12 and 13, respectively, and heavy chain CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 14, 15 and 16, respectively. In some examples, the antibody or antigen binding fragment thereof is administered every three weeks.

In one aspect, the disclosure provides use of an anti-programmed death 1 (anti-PD-1) antibody, or antigen binding fragment thereof in the manufacture of a medicament for treating cancer in a human patient, wherein about 280 mg to about 450 mg of the anti-PD-1 antibody, or antigen binding fragment thereof is to be administered subcutaneously to the patient every approximately three weeks, and wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises: (a) light chain (LC) complementarity determining regions (CDRs) LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 1, 2 and 3, respectively, and heavy chain (HC) CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 6, 7 and 8, respectively; or (b) light chain CDRs LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 11, 12 and 13, respectively and heavy chain CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 14, 15 and 16, respectively.

In examples of the disclosure, the antibody or antigen-binding fragment is pembrolizumab or an antigen-binding fragment thereof. In a further example, the anti-PD-1 antibody is pembrolizumab.

The disclosure also provides a method of treating cancer in a human patient comprising subcutaneously administering to the patient approximately every three weeks a dose of an anti-PD-1 antibody, or antigen binding fragment thereof, that is at least 1.6 times higher than a 200 mg or a 2 mg/kg dose of the anti-PD-1 antibody, or antigen binding fragment thereof, administered by an IV route of administration approximately every three weeks, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises (a) light chain (LC) complementarity determining regions (CDRs) LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 1, 2 and 3, respectively, and heavy chain (HC) CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 6, 7 and 8, respectively; or (b) light chain CDRs LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 11, 12 and 13, respectively, and heavy chain CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 14, 15 and 16, respectively. In some examples, the antibody or antigen binding fragment thereof is administered every three

weeks. In examples of the disclosure, the antibody or antigen-binding fragment is pembrolizumab or an antigen-binding fragment thereof. In a further example, the anti-PD-1 antibody is pembrolizumab.

The disclosure also provides a method of treating cancer in a human patient comprising subcutaneously administering to the patient approximately every three weeks a dose of an anti-PD-1 antibody, or antigen binding fragment thereof, that is at least 1.6 times higher than a 200 mg or a 2 mg/kg dose of the anti-PD-1 antibody, or antigen binding fragment thereof, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises (a) light chain (LC) complementarity determining regions (CDRs) LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 1, 2 and 3, respectively, and heavy chain (HC) CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 6, 7 and 8, respectively; or (b) light chain CDRs LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 11, 12 and 13, respectively, and heavy chain CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 14, 15 and 16, respectively. In some examples, the antibody or antigen binding fragment thereof is administered every three weeks.

In another aspect, the disclosure provides use of an anti-PD-1 antibody, or antigen binding fragment thereof in the manufacture of a medicament for treating cancer in a human patient, wherein at least 1.6 times higher than a 200 mg or a 2 mg/kg dose of the anti-PD-1 antibody, or antigen binding fragment thereof is to be administered subcutaneously to the patient approximately every three weeks, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises: (a) light chain (LC) complementarity determining regions (CDRs) LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 1, 2 and 3, respectively, and heavy chain (HC) CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 6, 7 and 8, respectively; or (b) light chain CDRs LC-CDR1, LC-CDR2 and LC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 11, 12 and 13, respectively, and heavy chain CDRs HC-CDR1, HC-CDR2 and HC-CDR3 comprising a sequence of amino acids as set forth in SEQ ID NOs: 14, 15 and 16, respectively.

In some examples of the disclosure, the antibody or antigen-binding fragment is pembrolizumab or an antigen-binding fragment thereof. In a further example, the anti-PD-1 antibody is pembrolizumab. In examples of the

methods described above, the bioavailability of the anti-PD-1 antibody, or antigen binding fragment thereof, is at least 63%. In examples of the methods described above, the bioavailability of the anti-PD-1 antibody, or antigen binding fragment thereof, is at least 64%. In examples of the methods described above, the bioavailability of the anti-PD-1 antibody, or antigen binding fragment thereof, is at least 66%.

In another aspect, the disclosure provides use of pembrolizumab in the manufacture of a medicament for treating cancer in a human patient, wherein about 280 mg to about 450 mg of pembrolizumab is to be administrated subcutaneously to the patient every approximately three weeks.

In another aspect, the disclosure provides use of pembrolizumab in the manufacture of a medicament for treating cancer, as defined herein.

In another aspect, the disclosure provides use of about 280 to 450 mg of pembrolizumab in the manufacture of a medicament for treating cancer as defined herein.

In another aspect, the disclosure provides pembrolizumab for use in treating cancer as defined herein.

In examples of the disclosure, the amount of anti-PD-1 antibody or antigen-binding fragment thereof administered to the patient is from 320 mg to 420 mg, from 340 mg to 420 mg, from 345 mg to 415 mg, from 350 mg to 410 mg, from 355 mg to 405 mg, from 360 mg to 400 mg, from 365 mg to 395 mg, from 370 mg to 390 mg, from 375 mg to 385 mg, or from 379 mg to 381 mg.

In examples of the disclosure, the amount of anti-PD-1 antibody or antigen-binding fragment thereof administered to the patient is from about 280 mg to about 450 mg. In further examples, the amount of antibody or antigen-binding fragment is about 300 mg to about 450 mg. In further examples, the amount of antibody or antigen-binding fragment is about 320 mg to about 450 mg. In further examples, the amount of antibody or antigen-

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examples, the amount of antibody or antigen-binding fragment is about 360 mg to about 390 mg. In further examples, the amount of antibody or antigen-binding fragment is about 370 mg to about 390 mg. In further examples, the amount of antibody or antigen-binding fragment is about 375 mg to about 390 mg. In further examples, the amount of antibody or antigen-binding
5 fragment is about 365 mg to about 395 mg. In further examples, the amount of antibody or antigen-binding fragment is about 375 mg to about 385 mg. In further examples, the amount of antibody or antigen-binding fragment is about 379 mg to about 381 mg. In further examples, the amount of antibody or antigen-binding fragment is about 380 mg. In further examples, the amount of antibody or antigen-binding fragment is 380 mg.

10 In one example, the amount of antibody or antigen binding fragment thereof administered is 280 mg. In one example, the amount of antibody or antigen binding fragment thereof administered is 285 mg. In another example, the amount of antibody or antigen binding fragment thereof administered is 320 mg. In another example, the amount of antibody or antigen binding fragment thereof administered is 340 mg. In another example, the amount of antibody or antigen binding fragment thereof administered is 360 mg. In another example, the amount of
15 antibody or antigen binding fragment thereof administered is 370 mg. In another example, the amount of antibody or antigen binding fragment thereof administered is 380 mg. In another example, the amount of antibody or antigen binding fragment thereof administered is 400 mg. In another example, the amount of antibody or antigen binding fragment thereof administered is
20 420 mg.

In all of the above treatment methods, compositions and uses herein, the anti-PD-1 antibody or antigen-binding fragment inhibits the binding of PD-L1 to PD-1, and preferably also inhibits the binding of PD-L2 to PD-1. In some examples of the treatment methods, compositions and uses of the disclosure, the anti-PD-1 antibody or antigen-binding fragment is a
25 monoclonal antibody, which specifically binds to PD-1 and blocks the binding of PD-L1 to PD-1. In one particular example, the anti-PD-1 antibody comprises a heavy chain and a light chain, wherein the light and heavy chains comprise the amino acid sequences shown in Figure 1 (SEQ ID NO:5 and SEQ ID NO:10).

In some examples of any of the above treatment methods, compositions and uses,
30 the cancer expresses one or both of PD-L1 and PD-L2. In some examples, PD-L1 expression is present or elevated in the cancer.

In another aspect, the disclosure provides a kit for treating a patient with cancer, the kit comprising: (a) a composition for subcutaneous injection comprising about 280 mg to about 450 mg of pembrolizumab, contained in one or more pre-filled syringes, and (b) instructions for using pembrolizumab, in the use as defined herein.

5

BRIEF DESCRIPTION OF THE DRAWINGS