individual when administered in combination with a PD-1 antagonist. In such embodiments, the TLR9 agonist is a CpG-C type oligonucleotide.

[0010] In a still further embodiment, the invention provides use of a PD-1 antagonist and a TLR9 agonist in the manufacture of medicaments for treating cancer in an individual, wherein the TLR9 agonist is a CpG-C type oligonucleotide. In some embodiments, the medicaments comprise a kit, and the kit also comprises a package insert comprising instructions for using the PD-1 antagonist in combination with the TLR9 agonist to treat cancer in an individual.

[0011] In a futher embodiment, the combination therapy of the methods, medicaments or kits discussed above further comprises an anti-IL-10 antibody.

[0011a] In a first aspect, there is provided use of a combination therapy which comprises a PD-1 antagonist and a TLR9 agonist in the manufacture of a medicament for treating cancer in an individual, wherein the TLR9 agonist is a CpG-C type oligonucleotide having a sequence consisting of 5'-TCGAACGTTCGAACGTTCGAACGTTCGAAT-3' (SEQ ID NO: 45), and wherein the PD-1 antagonist is: (i) a monoclonal antibody, or antigen binding fragment thereof, which comprises light chain CDRs of SEQ ID NOs: 7, 8 and 9 and heavy chain CDRs of SEQ ID NOs: 10, 11 and 12, or (ii) an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, and wherein the heavy chain comprises SEQ ID NO: 21 and the light chain comprises SEQ ID NO: 22.

[0011b] In a second aspect, there is provided use of a combination of compounds in the manufacture of a medicament for treating a human individual diagnosed with cancer, wherein the use comprises that at first pembrolizumab is to be administered to the individual, followed by intratumoral administration of an oligonucleotide consisting of SEQ ID NO: 45 three weeks later.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIGURE 1 shows amino acid sequences of the light chain and heavy chain CDRs for an exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NOs:1-6).

[0013] FIGURE 2 shows amino acid sequences of the light chain and heavy chain CDRs for another exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NOs:7-12).

[0014] FIGURE 3 shows amino acid sequences of the heavy chain variable region and full length heavy chain for an exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NO:13 and SEQ ID NO:14).

[0015] FIGURE 4 shows amino acid sequences of alternative light chain variable regions for an exemplary anti-PD-1 monoclonal antibody useful in the present invention (SEQ ID NOs:15-17).

[0016] FIGURE 5 shows amino acid sequences of alternative light chains for an exemplary anti-PD-1 monoclonal antibody useful in the present invention, with FIG. 5A showing the amino acid sequences for the K09A-L-11 and K09A-L-16 light chains (SEQ ID NOs:18 and 19, respectively) and FIG. 5B showing the amino acid sequence for the K09A-L-17 light chain (SEQ ID NO:20).

[0017] FIGURE 6 shows amino acid sequences of the heavy and light chains for pembrolizumab (SEQ ID NOs. 21 and 22, respectively).

CLAIMS

1. Use of a combination therapy which comprises a PD-1 antagonist and a TLR9 agonist in the manufacture of a medicament for treating cancer in an individual, wherein the TLR9 agonist is a CpG-C type oligonucleotide having a sequence consisting of 5'-TCGAACGTTCGAACGTTCGAACGTTCGAAT-3' (SEQ ID NO: 45), and wherein the PD-1 antagonist is:

   (i) a monoclonal antibody, or antigen binding fragment thereof, which comprises light chain CDRs of SEQ ID NOs: 7, 8 and 9 and heavy chain CDRs of SEQ ID NOs: 10, 11 and 12, or

   (ii) an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, and wherein the heavy chain comprises SEQ ID NO: 21 and the light chain comprises SEQ ID NO: 22.

2. The use of claim 1, wherein the CpG-C type oligonucleotide is an oligodeoxynucleotide with a phosphorothioate backbone.

3. Use of a combination of compounds in the manufacture of a medicament for treating a human individual diagnosed with cancer, wherein the use comprises that at first pembrolizumab is to be administered to the individual, followed by intratumoral administration of an oligonucleotide consisting of SEQ ID NO: 45 three weeks later.

4. The use of claim 3, comprising that 200 mg of pembrolizumab Q3W is to be administered to the individual starting on Day 1 and intratumoral administration of the oligonucleotide of SEQ ID NO: 45 at a dose of 2.0, 4.0 or 8.0 mg starting on Day 22 once a week for four weeks, followed by a dose of 2.0, 4.0 or 8.0 mg once every three weeks.

5. The use of claim 3 or 4, wherein the individual has not been previously treated with anti-PD-1 or anti-PD-L1 therapy or is confirmed progressive while receiving prior anti-PD-1 therapy.

6. The use of any one of claims 3 and 4, wherein the CpG-C type oligonucleotide is a sodium salt with a sequence consisting of 5'-TCGAACGTTCGAACGTTCGAACGTTCGAAT-3' (SEQ ID NO: 45), and the oligonucleotide is an oligodeoxynucleotide with a phosphorothioate backbone.

7. The use of claim 1, wherein the CpG-C type oligonucleotide has a sequence that consists of 5'-TCGTTCGAACGTTCGAACGTTCGAA-3' (SEQ ID NO:42).

8. The use of any one of claims 1 and 3-7, wherein the cancer is advanced or metastatic melanoma, renal cell carcinoma, non-small cell lung cancer, bladder cancer or colorectal cancer.

9. The use of claim 1, wherein the PD-1 antagonist is pembrolizumab and the CpG-C type oligonucleotide has a sequence consisting of 5'-TCGAACGTTCGAACGTTCGAACGTTCGAAT-3'(SEQ ID NO:45).

10. The use of claim 1, wherein the PD-1 antagonist is pembrolizumab and the CpG-C type oligonucleotide has a sequence consisting of 5'-TCGAACGTTCGAACGTTCGAACGTTCGAAT-3'(SEQ ID NO:45), and the oligonucleotide is an oligodeoxynucleotide with a phosphorothioate backbone.

11. The use of claim 9 or 10 wherein the cancer is selected from the group consisting of advanced or metastatic melanoma, renal carcinoma, NSCLC, bladder cancer and colorectal cancer.

12. The use of claim 1, wherein the PD-1 antagonist is pembrolizumab and the CpG-C type oligonucleotide has a sequence consisting of 5'-TCGTTCGAACGTTCGAACGTTCGAA-3' (SEQ ID NO:42).