METHODS, COMPOSITIONS, AND KITS FOR TREATMENT OF CANCER

RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Application No. 62/118,350, filed February 19, 2015, and U.S. Provisional Application No. 62/150,235, filed April 20, 2015, the disclosures of which are incorporated by reference herein in their entireties, including drawings.

BACKGROUND

[0002] The present application is directed to methods, compositions, and kits that utilize a combination of FGFR3 inhibitor and PD1 inhibitor to treat cancer.

SUMMARY

[0002a] In one aspect, the present disclosure refers to the use of an antagonistic FGFR3 antibody in the manufacture of a medicament for treating a solid tumor, wherein the antagonistic FGFR3 antibody is to be administered simultaneously or sequentially in combination with a therapeutically effective amount of an antibody or antigen-binding fragment thereof that inhibits PD1 activity by binding to PD1 or a ligand thereof. In one example, the present disclosure refers to the use of an antagonistic FGFR3 antibody in the manufacture of a medicament for treating a solid tumor, wherein the antagonistic FGFR3 antibody is to be administered simultaneously or sequentially in combination with a therapeutically effective amount of a PD1 antibody. In one example, there is disclosed the use of an antagonistic FGFR3 antibody in combination with a therapeutically effective amount of a PD1 inhibitor selected from the group consisting of a PD1 antibody, an antagonistic PDL2 antibody, a truncated form of PDL1, and a truncated form of PDL2, in the manufacture of a medicament for treating a solid tumor.

[0002b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising an antagonistic FGFR3 antibody and an antibody or antigen-binding fragment thereof that inhibits PD1 activity by binding to PD1 or a ligand thereof. In another example, the present disclosure refers to a pharmaceutical composition comprising an antagonistic FGFR3 antibody and a PD1 antibody. In another example, there is disclosed a pharmaceutical composition comprising an antagonistic FGFR3 antibody and a PD1 inhibitor selected from the group consisting of a PD1 antibody, an antagonistic PDL2 antibody, a truncated form of PDL1, and a truncated form of PDL2.

[0003] Provided herein in certain examples are methods of treating a solid or hematologic tumor in a subject in need thereof comprising administering a therapeutically effective amount of an FGFR3 inhibitor and a therapeutically effective amount of a PD1 inhibitor. In

certain examples, the FGFR3 inhibitor binds FGFR3. In other examples, the FGFR3 inhibitor binds a ligand for FGFR3. In certain examples, the FGFR3 inhibitor is an antagonistic FGFR3 antibody, and in certain of these examples the antagonistic FGFR3 antibody comprises one or more of a CDR-H1 comprising SEQ ID NO:1, a CDR-H2 comprising SEQ ID NO:2, a CDR-H3 comprising SEQ ID NO:3, a heavy chain variable region comprising SEQ ID NO:7, a heavy chain comprising SEQ ID NO:9, a CDR-L1 comprising SEQ ID NO:4, a CDR-L2 comprising SEQ ID NO:5, a CDR-L3 comprising SEQ ID NO:6, a light chain variable region comprising SEQ ID NO:8, and a light chain comprising the amino acid sequence set forth in SEQ ID NO:10. In certain of these examples, the FGFR3 antagonistic antibody is B-701. In other examples, the antagonistic FGFR3 antibody is selected from the group consisting of PRO-001 and IMC-D11. In certain examples, the FGFR3 inhibitor is a small molecule pan-FGFR inhibitor, and in certain of these examples the pan-FGFR inhibitor is selected from the group consisting of infigratinib, AZD4547, LY2874455, Debio 1347, ARQ 087, and JNJ-42756493. In certain examples, the PD1 inhibitor binds PD1. In other examples, the PD1 inhibitor binds a ligand for PD1. In certain examples, the PD1 inhibitor is an antagonistic PD1 antibody, and in certain of these examples the antagonistic PD1 antibody is selected from the group consisting of nivolumab, pembrolizumab, CT-011, MEDI-0680, and RMP1-14. In other examples, the PD1 inhibitor is an antagonistic PD1 ligand antibody, and in certain of these examples the antagonistic PD1 ligand antibody is selected from the group consisting of MEDI-4736, RG7446, BMS-936559, MSB0010718C, and MPDL3280A.

What is claimed is:

1. Use of an antagonistic FGFR3 antibody in the manufacture of a medicament for treating a solid tumor, wherein the antagonistic FGFR3 antibody is to be administered simultaneously or sequentially in combination with a therapeutically effective amount of an antibody or antigen-binding fragment thereof that inhibits PD1 activity by binding to PD1 or a ligand thereof.

2. The use of claim 1, wherein the antagonistic FGFR3 antibody comprises CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:1, CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:2, CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:3, and wherein the antagonistic FGFR3 antibody comprises CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:4, CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO:5, and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:6.

3. The use of claim 2, wherein the antagonistic FGFR3 antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO:7 and/or wherein the antagonistic FGFR3 antibody comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO:8.

4. The use of claim 1, wherein the antibody or antigen-binding fragment thereof that inhibits PD1 activity is an antagonistic PD1 antibody or an antagonistic PD1-binding fragment thereof.

5. The use of claim 4, wherein the antagonistic PD1 antibody is selected from the group consisting of nivolumab, pembrolizumab, CT-011, MEDI-0680, and RMP1-14.

6. The use of claim 1, wherein the antibody or antigen-binding fragment thereof that inhibits PD1 activity is an antagonistic PD1 ligand antibody or an antagonistic PD1 ligand-binding fragment thereof.

7. The use of claim 6, wherein the antagonistic PD1 ligand antibody is selected from the group consisting of MEDI-4736, RG7446, BMS-936559, MSB0010718C, and MPDL3280A.

8. A pharmaceutical composition comprising an antagonistic FGFR3 antibody and an antibody or antigen-binding fragment thereof that inhibits PD1 activity by binding to PD1 or a ligand thereof.

9. The composition of claim 8, further comprising a pharmaceutically acceptable carrier.

10. The composition of claim 9, wherein the antagonistic FGFR3 antibody comprises CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:1, CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:2, CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:3, and wherein the antagonistic FGFR3 antibody comprises CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:4, CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO:5, and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:6.

11. The composition of claim 10, wherein the antagonistic FGFR3 antibody comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO:7 and /or wherein the antagonistic FGFR3 antibody comprises a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO:8.

12. The composition of claim 8, wherein the antibody or antigen-binding fragment thereof that inhibits PD1 activity by binding to PD1 or a ligand thereof is an antagonistic PD1 antibody or an antagonistic PD1-binding fragment thereof.

13. The composition of claim 12, wherein the antagonistic PD1 antibody is selected from the group consisting of nivolumab, pembrolizumab, CT-011, MEDI-0680, and RMP1-14.

14. The composition of claim 8, wherein the antibody or antigen-binding fragment thereof that inhibits PD1 activity by binding to PD1 or a ligand thereofis an antagonistic PD1 ligand antibody.

15. The composition of claim 14, wherein the antagonistic PD1 ligand antibody is selected from the group consisting of MEDI-4736, RG7446, BMS-936559, MSB0010718C, and MPDL3280A.