than the patient's response to an immune checkpoint inhibitor in the absence of pre-treatment with an FGFR inhibitor.

[0002] According to particular examples, the present disclosure provides a method of treating cancer in a patient comprising administering a therapeutically effective amount of an immune checkpoint inhibitor to the patient, wherein the patient has an FGFR genetic variant (in particular a FGFR mutation or FGFR fusion), and has been treated with an FGFR inhibitor. Stated another way, the method may comprise administering an FGFR inhibitor to the patient for a period of time (e.g., as a monotherapy and/or without simultaneous administration of an immune checkpoint inhibitor), and after said period of time, administering an immune checkpoint inhibitor to the patient for a subsequent period of time (e.g., as a monotherapy and/or without simultaneous administration of an FGFR inhibitor). According to particular examples, the present disclosure provides an immune checkpoint inhibitor for use in the treatment of cancer in a patient, wherein the patient has an FGFR genetic variant (in particular a FGFR mutation or FGFR fusion), and has been treated with an FGFR inhibitor. Stated another way, the present disclosure provides an FGFR inhibitor for use in the treatment of cancer in a patient for a period of time (e.g., as a monotherapy and/or without simultaneous administration of an immune checkpoint inhibitor), and after said period of time, administering an immune checkpoint inhibitor to the patient for a subsequent period of time (e.g., as a monotherapy and/or without simultaneous administration of an FGFR inhibitor). According to particular examples, the present disclosure provides the use of an immune checkpoint inhibitor for the manufacture of a medicament for the treatment of cancer in a patient, wherein the patient has an FGFR genetic variant (in particular a FGFR mutation or FGFR fusion), and has been treated with an FGFR inhibitor. Stated another way, the present disclosure provides the use of an FGFR inhibitor for the manufacture of a medicament for the treatment of cancer in a patient for a period of time (e.g., as a monotherapy and/or without simultaneous administration of an immune checkpoint inhibitor), and after said period of time, administering an

FGFR3 genetic alterations and who progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

[0009] According to particular examples, the FGFR variant is selected from the group consisting of FGFR2:AFF3; FGFR2:BICC1; FGFR2:CASP7; FGFR2:CCDC6; FGFR2:OFD1; FGFR3:BAIAP2L1; FGFR3:TACC3-Intron; FGFR3:TACC3v1; FGFR3:TACC3v3; and a combination thereof; in particular FGFR2:BICC1; FGFR2:CASP7; FGFR3:BAIAP2L1; FGFR3:TACC3v1; FGFR3:TACC3v3 and a combination thereof.

[0010] According to particular examples, the FGFR variant is a FGFR3 mutation, in particular a FGFR 3 mutation selected from the group consisting of FGFR3 R248C; FGFR3 S249C; FGFR3 G370C; FGFR3 Y373C; and a combination thereof.

[0011] According to particular examples, the FGFR inhibitor is erdafitinib and is administered in an amount of between about 8 mg and about 9 mg daily.

[0012] According to particular examples, the method is effective in achieving a complete or partial response in the patient, e.g., in reducing a tumor volume in the patient and/or stopping or reducing disease progression.

[0012a] In another aspect, there is provided use of an FGFR inhibitor in the manufacture of a medicament for the treatment of bladder cancer or locally advanced or metastatic urothelial cancer, such cancer harboring one or more FGFR2 or FGFR3 mutations or fusions, in a patient diagnosed with such cancer, wherein the FGFR inhibitor is effective to sensitize the patient to an antibody that blocks the interaction between PD-1 and PD-L1, the use comprising: an FGFR inhibitor to be administered to the patient during a second period of time, wherein an antibody that blocks the interaction between PD-1 and PD-L1 is not administered during said second period of time; and after said second period of time, an antibody that blocks the interaction between PD-1 and PD-L1 to be administered to the patient during a third period of time, wherein an FGFR inhibitor is not administered to the patient during said third period of time, wherein the patient: (a) has been diagnosed with bladder cancer or locally advanced or metastatic urothelial cancer, such cancer harboring one or more FGFR2 or FGFR3 mutations or fusions, (b) was

administered a first antibody that blocks the interaction between PD-1 and PD-L1 during a first period of time prior to the second period of time, wherein an FGFR inhibitor was not administered to the patient during said first period of time, and (c) did not respond to the first antibody that blocks the interaction between PD-1 and PD-L1 during said first period of time; wherein the FGFR inhibitor is erdafitinib or a pharmaceutically acceptable salt thereof.

[0012b] In another aspect, there is provided use of a FGFR inhibitor in the manufacture of a medicament for sensitizing a bladder cancer patient or a locally advanced or metastatic urothelial cancer patient, such cancer harboring one or more FGFR2 or FGFR3 mutations or fusions, to an antibody that blocks the interaction between PD-1 and PD-L1, wherein the FGFR inhibitor is erdafitinib or a pharmaceutically acceptable salt thereof.

[0013] In the following passages, different aspects of the disclosure are defined in more detail. Each aspect so defined may be combined with any other aspect or aspects unless clearly indicated to the contrary. In particular, any feature indicated as being preferred or advantageous may be combined with any other feature or features indicated as being preferred or advantageous.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] Embodiments of the invention may be further understood when read in conjunction with the appended figures.

[0015] Fig. 1 is a graph illustrating response rate with prior systemic therapies.

[0016] Fig. 2 is a Kaplan-Meier plot of PFS following subsequent therapy to erdafitinib

[0017] Fig. 3 is a Kaplan-Meier plot of OS following subsequent therapy to erdafitinib.

What is claimed is:

1. Use of an FGFR inhibitor in the manufacture of a medicament for the treatment of bladder cancer or locally advanced or metastatic urothelial cancer, such cancer harboring one or more FGFR2 or FGFR3 mutations or fusions, in a patient diagnosed with such cancer, wherein the FGFR inhibitor is effective to sensitize the patient to an antibody that blocks the interaction between PD-1 and PD-L1, the use comprising:

an FGFR inhibitor to be administered to the patient during a second period of time, wherein an antibody that blocks the interaction between PD-1 and PD-L1 is not administered during said second period of time; and

after said second period of time, an antibody that blocks the interaction between PD-1 and PD-L1 to be administered to the patient during a third period of time, wherein an FGFR inhibitor is not administered to the patient during said third period of time, wherein the patient:

(a) has been diagnosed with bladder cancer or locally advanced or metastatic urothelial cancer, such cancer harboring one or more FGFR2 or FGFR3 mutations or fusions,

(b) was administered a first antibody that blocks the interaction between PD-1 and PD-L1 during a first period of time prior to the second period of time, wherein an FGFR inhibitor was not administered to the patient during said first period of time, and

(c) did not respond to the first antibody that blocks the interaction between PD-1 and PD-L1 during said first period of time;

wherein the FGFR inhibitor is erdafitinib or a pharmaceutically acceptable salt thereof.

2. The use according to claim 1, wherein the FGFR inhibitor is erdafitinib free base.

3. The use according to claim 1 or 2, wherein the patient responded to the FGFR inhibitor during said second period of time.

4. The use according to any of claims 1-3, wherein the antibody that blocks the interaction between PD-1 and PD-L1 is pembrolizumab, atezolizumab or nivolumab.

5. The use according to any of claims 1-3, wherein the antibody that blocks the interaction between PD-1 and PD-L1 is selected from the group consisting of atezolizumab, pembrolizumab, nivolumab, durvalumab, and avelumab.

6. The use according to any of claims 1-3, wherein the antibody that blocks the interaction between PD-1 and PD-L1 is cetrelimab.

7. The use according to any of claims 1-6, wherein the patient has been diagnosed with bladder cancer.

8. The use according to any of claims 1-6, wherein the patient has been diagnosed with locally advanced or metastatic urothelial cancer.

9. The use according to any of claims 1-6, wherein the patient has been diagnosed with locally advanced or metastatic urothelial cancer and who progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

10. The use according to any of claims 1-9, wherein the patient has one or more FGFR2 or FGFR3 mutations or fusions selected from the group consisting of FGFR2:AFF3; FGFR2:BICC1; FGFR2:CASP7; FGFR2:CCDC6; FGFR2:OFD1; FGFR3:BAIAP2L1; FGFR3:TACC3-Intron; FGFR3:TACC3v1; FGFR3:TACC3v3; and a combination thereof.

11. The use according to any of claims 1-10, wherein the FGFR inhibitor is erdafitinib and is to be administered in an amount of between 8 mg and 9 mg daily during said second period of time.

12. The use according to any of claims 1-11, wherein the use is effective in achieving a complete or partial response in the patient, e.g., in reducing a tumor volume in the patient and/or stopping or reducing disease progression.

13. Use of a FGFR inhibitor in the manufacture of a medicament for sensitizing a bladder cancer patient or a locally advanced or metastatic urothelial cancer patient, such cancer harboring one or more FGFR2 or FGFR3 mutations or fusions, to an antibody that blocks the interaction between PD-1 and PD-L1, wherein the FGFR inhibitor is erdafitinib or a pharmaceutically acceptable salt thereof.

14. Use according to claim 13, wherein the antibody that blocks the interaction between PD-1 and PD-L1 is pembrolizumab, atezolizumab or nivolumab.

15. Use according to claim 13, wherein the antibody that blocks the interaction between PD-1 and PD-L1 is selected from the group consisting of atezolizumab, pembrolizumab, nivolumab, durvalumab, and avelumab.

16. Use according to claim 13, wherein the antibody that blocks the interaction between PD-1 and PD-L1 is cetrelimab.

17. Use according to any of claims 13-16, wherein the patient has been diagnosed with bladder cancer

18. Use according to any of claims 13-16, wherein the patient has been diagnosed with locally advanced or metastatic urothelial cancer.

19. Use according to any of claims 13-16, wherein the patient has been diagnosed with locally advanced or metastatic urothelial cancer and who progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

20. Use according to any of claims 13-19, wherein the one or more FGFR2 or FGFR3 mutations of fusions is selected from the group consisting of FGFR2:AFF3; FGFR2:BICC1; FGFR2:CASP7; FGFR2:CCDC6; FGFR2:OFD1; FGFR3:BAIAP2L1;

FGFR3:TACC3-Intron; FGFR3:TACC3V1; FGFR3:TACC3V3; and a combination thereof.

21. Use according to any of claims 13-20, wherein the FGFR inhibitor is erdafitinib.

22. Use according to any of claims 13-20, wherein the FGFR inhibitor is erdafitinib and is to be administered in an amount of between 8 mg and 9 mg daily.

23. Use according to any one of claims 1-22, wherein the one or more FGFR2 or FGFR3 mutations or fusions is selected from the group consisting of FGFR2:BICC1; FGFR2:CASP7; FGFR3:BAIAP2L1; FGFR3:TACC3v1; FGFR3:TACC3v3; and a combination thereof.

24. Use according to claim 23, wherein the one or more FGFR2 or FGFR3 mutations or fusions is selected from the group consisting of FGFR3:BAIAP2L1; FGFR3:TACC3v1; FGFR3:TACC3v3; and a combination thereof.

25. Use according to any one of claims 1-24, wherein the one or more FGFR2 or FGFR3 mutations or fusions is a FGFR3 mutation selected from the group consisting of FGFR3 R248C; FGFR3 S249C; FGFR3 G370C; FGFR3 Y373C; and a combination thereof.