if one or more FGFR mutants including at least the FGFR2 SNP C383R are present in the sample.

[0005] Disclosed herein are methods of treating cholangiocarcinoma in a patient comprising: evaluating a biological sample from the patient for the presence of one or more FGFR mutants including at least the mutation FGFR3 R397C; or one or more FGFR mutants including at least the mutation FGFR3 L608F; or one or more FGFR mutants including at least the fusion FGFR2-TACC2; and treating the patient with an FGFR inhibitor if one or more FGFR mutants as described above are present in the sample.

[0006] Disclosed herein are methods of treating cholangiocarcinoma in a patient harboring the FGFR2 SNP C383R, or harboring the fusion FGFR2-BICC1; or harboring the fusion FGFR2-CCAR1; or harboring the fusion FGFR2-KIAA1598; or harboring the fusion DTWD2-FGFR2; or harboring the fusion ESR2-FGFR2; or harboring the fusion FGFR2-MGEA5; or harboring the fusion FGFR2-SBNO2; or harboring the mutation FGFR2 C390>YS; or harboring the mutation FGFR2 N549K; in particular harboring FGFR2 C383R, comprising administering a FGFR inhibitor to said patient. The patient may comprise one or more further FGFR mutants.

[0007] Disclosed herein are methods of treating cholangiocarcinoma in a patient harboring the mutation FGFR3 R397C, or harboring the mutation FGFR3 L608F, or harboring the fusion FGFR2-TACC2, comprising administering a FGFR inhibitor to said patient. The patient may comprise one or more further FGFR mutants.

[0008] Disclosed herein is a FGFR inhibitor for use in the treatment of cholangiocarcinoma in a patient harboring the FGFR2 SNP C383R, or harboring the fusion FGFR2-BICC1; or harboring the fusion FGFR2-CCAR1; or harboring the fusion FGFR2-KIAA1598; or harboring the fusion DTWD2-FGFR2; or harboring the fusion ESR2-FGFR2; or harboring the fusion FGFR2-MGEA5; or harboring the fusion FGFR2-SBNO2; or harboring the mutation FGFR2 C390>YS; or harboring the mutation FGFR2 N549K; in particular harboring FGFR2 C383R. The patient may comprise one or more further FGFR mutants.

[0009] In one aspect, disclosed herein is a FGFR inhibitor for use in the treatment of cholangiocarcinoma in a patient harboring the mutation FGFR3 R397C, or harboring the mutation FGFR3 L608F, or harboring the fusion FGFR2-TACC2. The patient may comprise one or more further FGFR mutants.

[0010] Disclosed herein is the use of a FGFR inhibitor in the manufacture of a medicament for the treatment of cholangiocarcinoma in a patient harboring the FGFR2 SNP C383R, or harboring the fusion FGFR2-BICC1; or harboring the fusion FGFR2-CCAR1; or harboring the fusion FGFR2-KIAA1598; or harboring the fusion DTWD2-FGFR2; or harboring the fusion ESR2-FGFR2; or harboring the fusion FGFR2-MGEA5;

FGFR mutants including at least the mutation FGFR3 L608F; or one or more FGFR mutants including at least the fusion FGFR2-TACC2 is detected. In another aspect, disclosed herein is the use of a FGFR inhibitor in the manufacture of a medicament for the treatment of cholangiocarcinoma in a patient wherein the patient is identified as being responsive to the treatment with the FGFR inhibitor by evaluating a biological sample that had been obtained from the patient for the presence of one or more FGFR mutants including at least the mutation FGFR3 R397C; or one or more FGFR mutants including at least the mutation FGFR3 L608F; or one or more FGFR mutants including at least the fusion FGFR2-TACC2, wherein the presence of one or more FGFR mutants including at least the mutation FGFR3 R397C; or one or more FGFR mutants including at least the mutation FGFR3 L608F; or one or more FGFR mutants including at least the fusion FGFR2-TACC2 is detected.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0016] Reference to a particular numerical value includes at least that particular value, unless the context clearly dictates otherwise. When a range of values is expressed, another embodiment includes from the one particular value and/or to the other particular value. Further, reference to values stated in ranges include each and every value within that range. All ranges are inclusive and combinable.

[0017] The following abbreviations are used throughout the specification: FGFR (fibroblast growth factor receptor); FFPET (Formalin-Fixed Paraffin-Embedded Tissue); SNP (single nucleotide polymorphism).

[0018] As used herein, “treating” and like terms refer to reducing the severity and/or frequency of cancer symptoms, eliminating cancer symptoms and/or the underlying cause of said symptoms, reducing the frequency or likelihood of cancer symptoms and/or their underlying cause, and improving or remediating damage caused, directly or indirectly, by cancer.

[0019] “Biological samples” refers to any sample from a patient in which cancerous cells can be obtained and detection of a FGFR mutant is possible. Suitable biological samples include, but are not limited to, blood, lymph fluid, bone marrow, a solid tumor sample, or any combination thereof. In some embodiments, the biological sample can be FFPET.

FGFR mutants

[0020] As used herein, the phrase "FGFR mutant" refers to a FGFR fusion gene, a FGFR single nucleotide polymorphism, a FGFR mutation or all of these. In an embodiment, the phrase "FGFR mutant" refers to a FGFR fusion gene, a FGFR single nucleotide polymorphism, or both. In an embodiment, the phrase "FGFR mutant" refers to a FGFR fusion gene. In an embodiment, the phrase "FGFR mutant" refers to a FGFR mutation.

[0021] "FGFR fusion" or "FGFR fusion gene" refers to a gene encoding FGFR (e.g., FGRF2 or FGFR3), or a portion thereof, and a fusion partner, or portion thereof, created by a translocation between the two genes. The presence of one or more FGFR fusion genes in a biological sample from a patient can be determined using the disclosed methods or using appropriate methods described in literature.

[0022] "FGFR single nucleotide polymorphism" (SNP) refers to a FGFR2 or FGFR3 gene in which a single nucleotide differs among individuals. A specific FGFR SNP in the methods of treatment or uses disclosed herein is FGFR2 C383R. The

CLAIMS

1. A FGFR inhibitor for use in the treatment of cholangiocarcinoma in a patient harboring the mutation FGFR3 R397C; or harboring the mutation FGFR3 L608F; or harboring the fusion FGFR2-TACC2.

2. Use of a FGFR inhibitor in the manufacture of a medicament for the treatment of cholangiocarcinoma in a patient wherein the patient is identified as being responsive to the treatment with the FGFR inhibitor by evaluating a biological sample that had been obtained from the patient for the presence of one or more FGFR mutants including at least the mutation FGFR3 R397C; or one or more FGFR mutants including at least the mutation FGFR3 L608F; or one or more FGFR mutants including at least the fusion FGFR2-TACC2, wherein the presence of one or more FGFR mutants including at least the mutation FGFR3 R397C; or one or more FGFR mutants including at least the mutation FGFR3 L608F; or one or more FGFR mutants including at least the fusion FGFR2-TACC2 is detected.

3. The FGFR inhibitor for use according to claim 1 or the use according to claim 2 wherein the FGFR inhibitor is erdafitinib.

4. The FGFR inhibitor for use or the use according to claim 3 wherein the erdafitinib is to be administered at a dose of 8 mg once daily.
5. The FGFR inhibitor for use or the use according to claim 3 wherein the erdafitinib is to be administered at a dose of 9 mg once daily.
6. The FGFR inhibitor for use or the use according to claim 3 wherein the erdafitinib is to be administered at a dose of 8 mg, in particular 8 mg once daily, with an option to uptitrate to 9 mg depending on serum phosphate levels (e.g. serum phosphate levels are < 5.5 mg/dL, or are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL), and depending on treatment-related adverse events observed.
7. The FGFR inhibitor for use or the use according to claim 6 wherein the levels of serum phosphate for determining whether or not to up-titrate are to be measured on a treatment day during the first cycle of erdafitinib treatment.
8. The FGFR inhibitor for use or the use according to claim 7 wherein the levels of serum phosphate for determining whether or not to up-titrate are to be measured on day 14 ± 2 days of the first cycle of erdafitinib treatment.

9. The FGFR inhibitor for use or the use according to claim 8 wherein the levels of serum phosphate for determining whether or not to up-titrate are to be measured on day 14 of the first cycle of erdafitinib treatment.
10. The FGFR inhibitor for use accrding to any one of claims 1 or 3 to 9 or the use according to any one of claims 2 to 9 wherein the patient is an Asian patient.