markers have been reported, that could help determine the dose and clinical outcomes in patients receiving anti-cancer treatments.

[0006] Recent introduction of targeted therapy and increasing numbers of available chemotherapeutic regimens, such as platinum and derivatives, taxanes and gemcitabine, do not effectively cure cancer patients, with varied response towards treatment and occurrence of drug toxicity. In addition, prognosis remains dismal in advanced cancer patients albeit careful evaluation of clinico-pathological factors that determine patient response to therapy, such as tumor, nodes and metastasis (TNM) staging, performance status, gender and weight loss.

[0007] Accordingly, there is a need for developing new therapeutic targets and pharmaceutical compositions for the treatment of cancer patients.

SUMMARY

[0008] In one aspect, the present invention refers to use of a histone-lysine N-methyltransferase EZH2 (enhancer of zeste homolog 2) inhibitor and an enhancer of interferon-gamma receptor activity in the manufacture of a pharmaceutical composition for treating cancer in a patient, wherein said inhibitor is selected from the group consisting of (-)-1-[(1R,4R,5S)-3-(Hydroxymethyl)-4,5-dihydroxy-2-cyclopenten-1-yl]4-aminoimidazo[4,5-c]pyridine hydrochloride (DZNep; 3-deazaneplanocin A); 1-{[4-amino-5-(2,2-dimethylpropanoyl)-1,3-thiazol-2-yl]sulfanyl}-3,3-dimethylbutan-2-one; 2-{[(3,4-dichlorophenyl)carbamoyl]amino}benzoic acid; (2E)-2-(1,3-benzothiazol-2-yl)-3-(4-chlorophenyl)prop-2-enenitrile; 1-(4-fluorophenyl)-3-(1-phenyl-5-propyl-1H-pyrazol-4-yl)urea; 5-(4-chlorophenyl)-3-(2,2-dichloroacetamido)thiophene-2-carboxamide; 3-(5-tert-butyl-1,2-oxazol-3-yl)-1-phenylurea; 1-benzoyl-3-2,3-dihydro-1H-inden-5-ylthiourea; N,5-diphenyl-1,3,4-oxadiazole-2-carboxamide; and 2,4-dihydroxy-5,7-diphenylpyrano[2,3-d]pyrimidin-8-ium perchlorate. In one example, the present disclosure describes use of a histone-lysine N-methyltransferase EZH2 (enhancer of zeste homolog 2) inhibitor and an enhancer of interferon-gamma receptor activity in the manufacture of a pharmaceutical composition for treating a patient having cancer, wherein said inhibitor is as defined in the attached set of claims.

In a another aspect, the present invention provides an *in vitro* method for determining susceptibility of a patient suffering from cancer to a treatment with a pharmaceutical composition as defined herein, wherein the method comprises, comparing a first level of EZH2 selected from the group consisting of EZH2 mRNA level in a tumor sample, EZH2 cDNA level made from mRNA from said tumor sample, and EZH2 protein level from said tumor sample, with a second level of EZH2 selected from the group consisting of EZH2 mRNA level from a non-tumor sample from said patient, EZH2 cDNA level made from mRNA from said non-tumor sample, and EZH2 protein level from said non-tumor sample; comparing a first level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level from said tumor sample, IFNGR1 cDNA level made from mRNA from said tumor sample, and IFNGR1 protein level from said tumor sample with the level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level from a non-tumor sample from said patient, IFNGR1 cDNA level made from mRNA from said non-tumor sample, and IFNGR1 protein level from said non-tumor sample; and wherein a patient characterized by an increased level of EZH2 in said tumor sample and a decreased level of IFNGR1 in said tumor sample is susceptible to a treatment with said pharmaceutical composition.

In a yet another aspect, the present invention provides an *in vitro* method for determining susceptibility of a patient suffering from advanced prostate cancer to a treatment with a pharmaceutical composition as defined herein, wherein the method comprises, comparing a first level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level in a tumor sample, IFNGR1 cDNA level made from mRNA

from said tumor sample, and IFNGR1 protein level from said tumor sample with the level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level from a non-tumor sample from said patient, IFNGR1 cDNA level made from mRNA from said non-tumor sample, and IFNGR1 protein level from said non-tumor sample; and wherein a patient characterized by a decreased level of IFNGR1 in said tumor sample is susceptible to a treatment with said pharmaceutical composition.

In a yet another aspect, the present invention provides an *in vitro* method for determining susceptibility of a patient suffering from breast cancer to a treatment with a pharmaceutical composition as defined herein, wherein the method comprises, comparing a first level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level in a tumor sample, IFNGR1 cDNA level made from mRNA from said tumor sample, and IFNGR1 protein level from said tumor sample with the level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level from a non-tumor sample from said patient, IFNGR1 cDNA level made from mRNA from said non-tumor sample, and IFNGR1 protein level from said non-tumor sample; wherein a patient suffering from basal breast cancer is characterized by an increased level of INFGR1 in said tumor sample is not susceptible to a treatment with said pharmaceutical composition; and wherein a patient suffering from luminal breast cancer is characterized by a decreased level of INFGR1 in said tumor sample is susceptible to a treatment with said pharmaceutical composition.

In one aspect, the present invention provides an *in vitro* method for making a prognosis with respect to the clinical outcome of a patient suffering from cancer comprising, comparing a first level of EZH2 selected from the group consisting of EZH2 mRNA level in a tumor sample, EZH2 cDNA level made from mRNA from said tumor sample, and EZH2 protein level from said tumor sample, with a second level of EZH2 selected from the group consisting of EZH2 mRNA level from a non-tumor sample from said patient, EZH2 cDNA level made from mRNA from said non-tumor sample, and EZH2 protein level from said non-tumor sample; comparing a first level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level from said tumor sample, IFNGR1 cDNA level made from mRNA from said tumor sample, and IFNGR1 protein level from said tumor sample with the level of IFNGR1 selected from the group consisting of IFNGR1 mRNA level from a non-tumor sample from said patient, IFNGR1 cDNA level made from mRNA from said non-tumor sample, and IFNGR1 protein level from said non-tumor sample; and making a prognosis with respect to the clinical outcome of a patient suffering from cancer.

In a further aspect, the present invention provides a pharmaceutical composition comprising a histone-lysine N-methyltransferase EZH2 (enhancer of zeste homolog 2) inhibitor and an enhancer of interferon-gamma receptor activity, wherein the inhibitor is defined in the attached set of claims.

In one example, the present disclosure provides a pharmaceutical composition

Claims

1. Use of a histone-lysine N-methyltransferase EZH2 (enhancer of zeste homolog 2) inhibitor and an enhancer of interferon-gamma receptor activity in the manufacture of a pharmaceutical composition for treating cancer in a patient, wherein said inhibitor is selected from the group consisting of (-)-1-[(1R,4R,5S)-3-(Hydroxymethyl)-4,5-dihydroxy-2-cyclopenten-1-yl]4-aminoimidazo[4,5-c]pyridine hydrochloride (DZNep; 3-deazaneplanocin A);
1-{[4-amino-5-(2,2-dimethylpropanoyl)-1,3-thiazol-2-yl]sulfanyl}-3,3-dimethylbutan-2-one;
2-{[(3,4-dichlorophenyl)carbamoyl]amino}benzoic acid;
(2E)-2-(1,3-benzothiazol-2-yl)-3-(4-chlorophenyl)prop-2-enenitrile;
1-(4-fluorophenyl)-3-(1-phenyl-5-propyl-1H-pyrazol-4-yl)urea;
5-(4-chlorophenyl)-3-(2,2-dichloroacetamido)thiophene-2-carboxamide;
3-(5-tert-butyl-1,2-oxazol-3-yl)-1-phenylurea;
1-benzoyl-3-2,3-dihydro-1H-inden-5-ylthiourea;
N,5-diphenyl-1,3,4-oxadiazole-2-carboxamide; and
2,4-dihydroxy-5,7-diphenylpyrano[2,3-d]pyrimidin-8-ium perchlorate.

2. The use of claim 1, wherein the interferon-gamma receptor is interferon-gamma receptor 1 (IFNGR1) encoding for interferon-gamma receptor (IFNGR1) subunit 1.

3. The use according to claim 1 or claim 2, the pharmaceutical composition further comprising one or more pharmaceutically acceptable excipients, vehicles or carriers.

4. The use of any of the preceding claims, wherein said inhibitor is (-)-1-[(1R,4R,5S)-3-(Hydroxymethyl)-4,5-dihydroxy-2-cyclopenten-1-yl]4-aminoimidazo[4,5-c]pyridine hydrochloride (DZNep; 3-deazaneplanocin A).