

mRNA expression of tumor vs normal, (referred as mRNA TvN fold change);

- wholly or partially sequencing genes of Table 1 or 9, thereby identifying the presence of activating mutation in the tumor sample ;

5 - for each intervention point of the group or subgroup of intervention points, determining the level of miRNAs of the genes of the intervention point as disclosed in Table 1 or 9, thereby determining a fold change of miRNAs level of tumor vs normal, (referred as miRNA TvN fold change);

10 - optionally, for each intervention point of the group or subgroup of intervention points, determining the copy number variation of the genes of the intervention point as disclosed in Table 1 or 9, thereby determining a tumor vs normal fold change for the amplified genes;

- calculating a score for each pathway based on the characterization data, wherein

15 - if, in the tumor sample, the presence of an activating mutation of a gene of an intervention point is detected, then a maximal score is given to the intervention point, in particular a score of 10 if the scoring is from 1 to 10;

20 - a score, preferably from 1 to 10, is calculated based on the arithmetic mean of the mRNA TvN fold changes of the genes for each intervention point of the group or subgroup of intervention points, provided that the mRNA TvN fold change of a gene is taken into consideration only if its value is at least 1.3; and

- the score of each intervention point of the group or subgroup of intervention points is either

25 a) the sum of the score due to the presence of an activating mutation and the score calculated by the average of the mRNA TvN fold changes; or

 b) the score due to the presence of an activating mutation if there is a mutation or the score calculated based on the arithmetic mean of the mRNA TvN fold changes in absence of mutation; and

30 - classifying the intervention points according to the calculated scores.

anti PD1L + MEK inhibitor + angiogenesis inhibitor

anti PD1L + MEK inhibitor + MET inhibitor

anti PD1L + MEK inhibitor + CDK4,6 inhibitor

anti CTLA4 + MEK inhibitor + MtorPI3K dual inhibitor

5 anti CTLA4 + MEK inhibitor + MET inhibitor

anti CTLA4 + MEK inhibitor + angiogenesis inhibitor, and

anti CTLA4 + MEK inhibitor + CDK4,6 inhibitor, wherein the drug combination is selected by the method disclosed above.

Preferably, the drugs included in the combination are selected from those disclosed in Table

10 1. More preferably, the drugs combination is selected in the group consisting of

Medi-4736 (Astra Zeneca) + MLN2480 (Takeda) + PF-384 (Pfizer)

Medi-4736 (Astra Zeneca) + MLN2480 (Takeda) + Axitinib (Pfizer) or Motesanib (Takeda)

Medi-4736 (Astra Zeneca) + MLN2480 (Takeda) + Crizotinib (Pfizer)

15 Medi-4736 (Astra Zeneca) + MLN2480 (Takeda) + Palbociclib (Pfizer)

Tremelimumab (Astra Zeneca) + MLN2480 (Takeda) + PF-384 (Pfizer)

Tremelimumab (Astra Zeneca) + MLN2480 (Takeda) + Axitinib (Pfizer) or Motesanib (Takeda)

Tremelimumab (Astra Zeneca) + MLN2480 (Takeda) + Crizotinib (Pfizer)

20 Tremelimumab (Astra Zeneca) + MLN2480 (Takeda) + Palbociclib (Pfizer)

Medi-4736 (Astra Zeneca) + Selumetinib (Astra Zeneca) + PF-384 (Pfizer)

Medi-4736 (Astra Zeneca) + Selumetinib (Astra Zeneca) + Axitinib (Pfizer) or Motesanib (Takeda)

Medi-4736 (Astra Zeneca) + Selumetinib (Astra Zeneca) + Crizotinib (Pfizer)

25 Medi-4736 (Astra Zeneca) + Selumetinib (Astra Zeneca) + Palbociclib (Pfizer)

Tremelimumab (Astra Zeneca) + Selumetinib (Astra Zeneca) + PF-384 (Pfizer)

Tremelimumab (Astra Zeneca) + Selumetinib (Astra Zeneca) + Crizotinib (Pfizer)

Tremelimumab (Astra Zeneca) + Selumetinib (Astra Zeneca) + Axitinib (Pfizer)

30 or Motesanib (Takeda), and

Tremelimumab (Astra Zeneca) + Selumetinib v + Palbociclib (Pfizer).

Preferably, the cancer is a lung cancer, more preferably a NSCLC.

CLAIMS

1- A method for determining in a patient having a cancer a classification of intervention points according to their activation status, wherein

- 5 - the intervention points comprise the group consisting of the HER, CDK4,6, PLK/AURK/Kinesins, Angiogenesis, Angiopoietins, Immune Modulators, PI3K, MET, MEK, ERK, Anti-Apoptosis, FGF, mTOR, Ras/Raf, Telomerase, IGF/glycolysis, Wnt, PARP, HDAC, JAK-STAT, Hedgehog, NOTCH pathway, DNA Repair and Others' (namely RET, ALK, ROS1 and UB1), or any subgroup thereof of at least 10 intervention points; and the genes of each intervention point are defined according to Table 1 or 9;
- 10 - the method comprises
 - characterizing a tumor sample in comparison to a normal histologically matched sample from the same patient, including
 - 15 - for each pathway of the group or subgroup of intervention points, determining the mRNA expression level of the genes of the intervention point as disclosed in Table 1 or 9, thereby determining a fold change of mRNA expression of tumor vs normal, (referred as mRNA TvN fold change);
 - 20 - wholly or partially sequencing genes of Table 1 or 9, thereby identifying the presence of activating mutation in the tumor sample ;
 - for each intervention point of the group or subgroup of intervention points, determining the level of miRNAs of the genes of the intervention point as disclosed in Table 1 or 9, thereby determining a fold change of miRNAs level of tumor vs normal, (referred as miRNA TvN fold change);
 - 25 - optionally, for each intervention point of the group or subgroup of intervention points, determining the copy number variation of the genes of the intervention point as disclosed in Table 1 or 9, thereby determining a tumor vs normal fold change for the amplified genes;
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10- A method for selecting a combination of three drugs useful for treating a patient having a cancer, wherein a group of three activated or disturbed intervention points are selected by the method of claim 9 and a drug is selected for each or disturbed intervention point, thereby providing a combination of three drugs.

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11- Use of a kit for classifying pathways according to their activation status, wherein the kit comprises means for measuring the mRNA expression level of the genes of Table 1 or 9 for intervention points comprising the group consisting of the HER, CDK4,6, PLK/AURK/Kinesins, Angiogenesis, Angiopoietins, Immune Modulators, PI3K, MET, MEK, ERK, Anti-Apoptosis, FGF, mTOR, Ras/Raf, Telomerase, IGF/glycolysis, Wnt, PARP, HDAC, JAK-STAT, Hedgehog, NOTCH pathway, DNA Repair and Others' (namely RET, ALK, ROS1 and UB1), or any subgroup thereof of at least 10 intervention points; means for detecting the mutations of Table 10; means for measuring the miRNA level of miRNA of Table 11 for intervention points comprising the group consisting of the HER, CDK4,6, PLK/AURK/Kinesins, Angiogenesis, Angiopoietins, Immune Modulators, PI3K, MET, MEK, ERK, Anti-Apoptosis, FGF, mTOR, Ras/Raf, Telomerase, IGF/glycolysis, Wnt, PARP, HDAC, JAK-STAT, Hedgehog, NOTCH, DNA Repair and Others' (namely RET, ALK, ROS1 and UB1), or any subgroup thereof of at least 10 intervention points.

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12- The use of claim 11, wherein the kit further comprises means for determining the copy number variation of the genes of Table 1 or 9 for pathways comprising the group consisting of the HER, CDK4,6, PLK/AURK/Kinesins, Angiogenesis, Angiopoietins, Immune Modulators, PI3K, MET, MEK, ERK, Anti-Apoptosis, FGF, mTOR, Ras/Raf, Telomerase, IGF/glycolysis, Wnt, PARP, HDAC, JAK-STAT, Hedgehog, NOTCH, DNA Repair and Others' (namely RET, ALK, ROS1 and UB1), or any subgroup thereof of at least 10 intervention points.

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13- Use of a drugs combination in the preparation of a medicament for the treatment of cancer, wherein the drugs combination is selected among the combinations disclosed in Table 6, Table 7, Table 8 or selected in the group consisting of

- 5 anti PD1L + Pan RAF inhibitor + MtorPI3K inhibitor
- anti PD1L + Pan RAF inhibitor + angiogenesis inhibitor
- anti PD1L + Pan RAF inhibitor + MET inhibitor
- anti PD1L + Pan RAF inhibitor + CDK4,6 inhibitor
- anti CTLA4 + Pan RAF inhibitor + MtorPI3K inhibitor
- anti CTLA4 + Pan RAF inhibitor + angiogenesis inhibitor
- 10 anti CTLA4 + Pan RAF inhibitor + MET inhibitor
- anti CTLA4 + Pan RAF inhibitor + CDK4,6 inhibitor
- anti PD1L + MEK inhibitor + MtorPI3K dual inhibitor
- anti PD1L + MEK inhibitor + angiogenesis inhibitor
- anti PD1L + MEK inhibitor + MET inhibitor
- 15 anti PD1L + MEK inhibitor + CDK,-6 inhibitor
- anti CTLA4 + MEK inhibitor + MtorPI3K dual inhibitor
- anti CTLA4 + MEK inhibitor + MET inhibitor
- anti CTLA4 + MEK inhibitor + angiogenesis inhibitor, and
- anti CTLA4 + MEK inhibitor + CDK4,6 inhibitor; and wherein the drug
- 20 combination is selected by the method according to claim 10.

14- The use according to claim 13, wherein the drugs combination is selected in the group consisting of

- Medi-4736 + MLN2480 + PF-384
- Medi-4736 + MLN2480 + Axitinib or Motesanib
- 25 Medi-4736 + MLN2480 + Crizotinib
- Medi-4736 + MLN2480 + Palbociclib
- Tremelimumab + MLN2480 + PF-384
- Tremelimumab + MLN2480 + Axitinib or Motesanib
- Tremelimumab + MLN2480 + Crizotinib
- 30 Tremelimumab + MLN2480 + Palbociclib
- Medi-4736 + Selumetinib + PF-384
- Medi-4736 + Selumetinib + Axitinib or Motesanib