CLAIMS

We claim:

1. ~~A method of treating a solid tumor in a subject comprising~~

~~(a) determining the presence or absence of a H-Ras mutation in a sample from said subject, and subsequently~~

~~(b) administering~~ Use of a therapeutically effective amount of a farnesyltransferase inhibitor ~~(FTI)~~ in the manufacture of a medicament for treating a H-Ras mutant head and neck squamous cell carcinoma (HNSCC) in a subject, ~~to said subject if said sample is determined to have a H-Ras mutation.~~wherein the HNSCC is at an advanced stage, metastatic, relapsed or refractory, and wherein the subject is a human.

2. The use of claim 1, wherein the HNSCC is human papillomavirus (HPV)-negative.

3. The use of claim 1, wherein the HNSCC is at an advanced stage.

4. The use of claim 1, wherein the HNSCC is metastatic.

5. The use of claim 1, wherein the HNSCC is relapsed or refractory.

~~2~~6. The ~~method of claim 1~~use of any one of claims 1-5, wherein ~~said~~the H-Ras mutation of the subject comprises an amino acid substitution at a codon selected from ~~a~~the group consisting of G12, G13, and Q61~~, and any combination thereof~~.

~~3. The method of claim 1 or 2, further comprising determining the presence or absence of a K-Ras mutation or a N-Ras mutation, wherein said sample does not have K-Ras mutation or N-Ras mutation.~~

~~4. The method of claim 3, wherein said sample has wild type K-Ras and wild type N-Ras.~~

7. The use of claim 6, wherein the H-Ras mutation is determined in a sample from the subject.

~~5~~8. The ~~method~~use of ~~any one of claims 1 to 4~~ claim 7, wherein ~~said~~the sample is a tissue biopsy~~.~~, or

~~6. The method of any one of claims 1 to 4, wherein said sample is~~ a tumor biopsy.

~~7. The method of any one of claims 1 to 6, wherein determining the presence or absence of a Ras mutation comprising analyzing nucleic acids obtained from said sample.~~

~~8~~9. The ~~method~~use of claim 0~~7~~, wherein ~~said~~the H- Ras mutation is determined by a method selected from the group consisting of sequencing, Polymerase Chain Reaction (PCR), DNA microarray, Mass Spectrometry (MS), Single Nucleotide Polymorphism (SNP) assay, denaturing high-performance liquid chromatography (DHPLC), ~~or~~and Restriction Fragment Length Polymorphism (RFLP) assay.

10. The use of any one of claims 1-9, wherein the amount of FTI contained in the medicament is suitable for administering at a dose of 1-1000 mg/kg body weight.

11. The use of any one of claims 1-9, wherein the amount of FTI contained in the medicament is suitable for administering twice a day.

~~9. The method of claim 8, wherein Ras mutation is determined by PCR.~~

~~10. The method of claim 8, wherein Ras mutation is determined by sequencing.~~

~~11. The method of any one of claims 1 to 6, wherein determining the presence or absence of a Ras mutation comprising analyzing proteins obtained from said sample.~~

~~12. The method of any one of claims 1 to 11, wherein said cancer is a hematological cancer or a solid tumor.~~

~~13. The method of claim 12, wherein said cancer is HPV negative.~~

~~14. The method of claim 12, wherein said cancer is at an advanced stage or metastatic.~~

~~15. The method of claim 12, wherein said cancer is a solid tumor selected from the group consisting of hepatocelluar carcinoma, head and neck cancer, salivary gland tumor, thyroid tumor, urothelial cancer, breast cancer, melanoma, gastric cancer, pancreatic cancer, and lung cancer.~~

~~16. The method of claim 13, wherein said cancer is head and neck cancer.~~

~~17. The method of claim 16, wherein said head and neck cancer is head and neck squamous cell carcinoma (HNSCC).~~

~~18. The method of claim 17, wherein the HNSCC is HPV negative HNSCC.~~

~~19. The method of claim 17 or 18, wherein said HNSCC is relapsed/refractory HNSCC.~~

~~20. The method of claim 13, wherein said cancer is salivary gland tumor.~~

~~21. The method of claim 20, wherein said salivary gland tumor is advanced salivary gland tumor.~~

~~22. The method of claim 13, wherein said cancer is thyroid tumor.~~

~~23. The method of claim 21, wherein said thyroid tumor is malignant thyroid tumor, or advanced thyroid tumor.~~

~~24. The method of claim 12, wherein the cancer is a hematological cancer selected from the group consisting of myeloproliferative neoplasm (MPN), myelodysplastic syndrome (MDS), chronic myelomonocytic leukemia (CMML), acute myeloid leukemia (AML), natural killer cell lymphoma (NK lymphoma), natural killer cell leukemia (NK leukemia), cutaneous T-Cell lymphoma (CTCL), peripheral T-cell lymphoma (PTCL), and chronic myeloid leukemia (CML).~~

~~25. A method of treating a malignant thyroid tumor in a subject comprising (a) determining the presence or absence of a H-Ras mutation in a sample of the thyroid tumor in said subject, and subsequently~~

~~(b) administering a therapeutically effective amount of tipifarnib to said subject if said sample is determined to have a H-Ras mutation.~~

~~26. A method of treating HNSCC in a subject comprising (a) determining the presence or absence of a H-Ras mutation in a sample of the HNSCC in said subject, and subsequently~~

~~(b) administering a therapeutically effective amount of tipifarnib to said subject if said sample is determined to have a H-Ras mutation.~~

~~27. A method of treating a salivary gland tumor in a subject comprising (a) determining the presence or absence of a H-Ras mutation in a sample from said salivary gland tumor in said subject, and subsequently~~

~~(b) administering a therapeutically effective amount of tipifarnib to said subject if said sample is determined to have a H-Ras mutation.~~

~~28. A method of treating a cancer in a subject comprising~~

~~(a) determining the presence or absence of a Ras mutation in a sample from said subject, said Ras mutation comprising a K-Ras mutation or a N-Ras mutation, and subsequently~~

~~(b) administering a therapeutically effective amount of a farnesyltransferase inhibitor (FTI) to said subject if said sample is determined to lack said K-Ras mutation or said N-Ras mutation.~~

~~29. The method of claim 28, wherein said Ras mutation comprises a K-Ras mutation.~~

~~30. The method of claim 28, wherein said Ras mutation comprises an N-Ras mutation.~~

~~31. The method of claim 28, wherein said Ras mutation comprises a K-Ras mutation and an N-Ras mutation.~~

~~32. The method of any one of claims 28 to 31, wherein said K-Ras mutation comprises an amino acid substitution at a codon selected from a group consisting of G12, G13, Q61, and any combination thereof.~~

~~33. The method of any one of claims 28 to 31, wherein said N-Ras mutation comprises an amino acid substitution at a codon selected from a group consisting of G12, G13, Q61, and any combination thereof.~~

~~34. The method of any one of claims 28 to 33, wherein said Ras mutation comprises an amino acid substitution at G12, G13, and Q61 in K-Ras; and an amino acid substitution at G12, G13, and Q61 in N-Ras mutation.~~

~~35. The method of any one of claims 28 to 33, wherein said sample does not have K-Ras mutation or N-Ras mutation.~~

~~36. The method of claim 35, wherein said sample has wild type K-Ras.~~

~~37. The method of claim 35, wherein said sample has wild type N-Ras.~~

~~38. The method of claim 35, wherein said sample has wild type K-Ras and wild type N-Ras.~~

~~39. The method of any one of claims 28 to 38, wherein said Ras mutation further comprises an H-Ras mutation, and said sample is determined to have said H-Ras mutation.~~

~~40. The method of claim 39, wherein said H-Ras mutation comprises an amino acid substitution at a codon selected from a group consisting of G12, G13, Q61, and any combination thereof.~~

~~41. The method of any one of claims 28 to 40, wherein said sample is a tissue biopsy.~~

~~42. The method of any one of claims 28 to 40, wherein said sample is a tumor biopsy.~~

~~43. The method of any one of claims 28 to 40, wherein said sample is a blood sample, a serum sample, or a bone marrow sample.~~

~~44. The method of any one of claims 28 to 43, wherein determining the presence or absence of a Ras mutation comprising analyzing nucleic acids obtained from said sample.~~

~~45. The method of claim 44, wherein said Ras mutation is determined by sequencing, Polymerase Chain Reaction (PCR), DNA microarray, Mass Spectrometry (MS), Single Nucleotide Polymorphism (SNP) assay, denaturing high-performance liquid chromatography (DHPLC), or Restriction Fragment Length Polymorphism (RFLP) assay.~~

~~46. The method of claim 45, wherein Ras mutation is determined by PCR.~~

~~47. The method of claim 45, wherein Ras mutation is determined by sequencing.~~

~~48. The method of any one of claims 28 to 43, wherein determining the presence or absence of a Ras mutation comprising analyzing proteins obtained from said sample.~~

49. The method of any one of claims 28 to 48, wherein said cancer is myeloproliferative neoplasm (MPN), myelodysplastic syndrome (MDS), chronic myelomonocytic leukemia (CMML), acute myeloid leukemia (AML), natural killer cell lymphoma (NK lymphoma), natural killer cell leukemia (NK leukemia), cutaneous T-Cell lymphoma (CTCL), peripheral T-cell lymphoma (PTCL), chronic myeloid leukemia (CML) or a solid tumor.

50. The method of claim 49, wherein said cancer is MDS.

51. The method of claim 50, wherein said MDS is lower risk MDS.

52. The method of claim 49, wherein said cancer is CMML.

53. The method of claim 52, wherein said CMML is low risk CMML or intermediate risk CMML.

54. The method of claim 52, wherein said CMML is myelodysplastic CMML or myeloproliferative CMML.

55. The method of claim 49, wherein said cancer is AML.

56. The method of claim 55, wherein said subject is post remission induction or post transplantation.

57. The method of claim 55, wherein said subject is over age 60 or otherwise unfit for remission induction.

58. The method of claim 49, wherein said cancer is a solid tumor selected from the group consisting of hepatocelluar carcinoma, head and neck cancer, salivary gland tumor, thyroid tumor, breast cancer, melanoma, gastric cancer, pancreatic cancer, and lung cancer.

59. A method of treating CMML in a subject comprising (a) determining said subject to have wild type K-Ras, and subsequently (b) administering a therapeutically effective amount of tipifarnib to said subject.

~~61. A method of treating CMML in a subject comprising (a) determining said subject to have wild type N-Ras, and subsequently (b) administering a therapeutically effective amount of tipifarnib to said subject.~~

~~62. A method of treating CMML in a subject comprising (a) determining said subject to have wild type K-Ras and wild type N-Ras, and subsequently(b) administering a therapeutically effective amount of tipifarnib to said subject.~~

~~63. A method of treating cancer in a subject comprising (a) KIR typing said subject, wherein said subject is a carrier of KIR2DS2 or KIR2DS5, and (b) administering a therapeutically effective amount of a FTI to said subject.~~

~~63. The method of claim 62 wherein said subject is a carrier of KIR2DS2.~~

~~64. The method of claim 62 wherein said subject is a carrier of KIR2DS5.~~

~~65. The method of any one of claims 62 to 64 further comprising HLA typing said subject, wherein said subject is a carrier of HLA-C2.~~

~~66. The method of claim 65, wherein said subject is a carrier of KIR2DS2 and HLA-C2.~~

~~67. The method of claim 65 or 66, wherein said carrier of HLA-C2 is homozygous for HLA-C2.~~

~~68. The method of any one of claims 62 to 67, wherein KIR typing comprises determining the presence of a KIR gene in a sample from said subject, wherein said KIR gene is selected from the groups consisting of KIR2DS2, KIR2DL2, KIR2DS5 and KIR2DL5.~~

~~69. The method of any one claims 62 to 67, wherein KIR typing and HLA typing is performed by sequencing, Polymerase Chain Reaction (PCR), DNA microarray, Mass Spectrometry (MS), Single Nucleotide Polymorphism (SNP) assay, Immunoblotting assay, or Enzyme-Linked Immunosorbent Assay (ELISA).~~

~~70. The method of claim 69, wherein KIR typing is performed by SNP analysis using MS.~~

~~71. The method of any one of claims 68 to 70, wherein said sample is a blood sample or a bone marrow sample.~~

72. The method of any one of claims 68 to 70, wherein said sample is peripheral blood mononuclear cells (PBMC).

73. The method of any one of claims 68 to 70, wherein said sample is enriched NK cells.

74. A method of treating cancer in a subject comprising

(a) determining expression level of a biomarker selected from the group consisting of KIR2DS2, KIR2DL2, KIR2DS5, KIR2DL5, and GZMM in a sample from said subject, wherein

(i) the expression level of KIR2DS2 in the sample is higher than a reference expression level of KIR2DS2;

(ii) the expression level of KIR2DL2 in the sample is lower than a reference expression level of KIR2DL2;

(iii) the expression level of KIR2DS5 in the sample is higher than a reference expression level of KIR2DS5;

(iv) the expression level of KIR2DL5 in the sample is lower than a reference expression level of KIR2DL5; or

(v) the expression level of GZMM in the sample is higher than a reference expression level of GZMM; and

(b) administering a therapeutically effective amount of an FTI to said subject.

75. A method of treating cancer in a subject comprising

(a) determining expression levels of KIR2DS2 and KIR2DL2, or KIR2DS5 and KIR2DL5 in a sample from said subject, wherein

(i) the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample is higher than a reference ratio; or

(ii) the ratio of the expression level of KIR2DS5 to the expression level of KIR2DL5 in the sample is higher than a reference ratio; and

(b) administering a therapeutically effective amount of an FTI to said subject.

76. The method of claim 74 comprising determining expression level of KIR2DS2, wherein the expression level of KIR2DS2 in the sample is higher than a reference expression level of KIR2DS2.

77. The method of claim 74 comprising determining expression level of KIR2DL2, wherein the expression level of KIR2DL2 in the sample is lower than a reference expression level of KIR2DL2.

78. The method of claim 74 comprising determining expression level of KIR2DS5, wherein the expression level of KIR2DS5 in the sample is higher than a reference expression level of KIR2DS5.

79. The method of claim 74 comprising determining expression level of KIR2DL5, wherein the expression level of KIR2DL5 in the sample is lower than a reference expression level of KIR2DL5.

80. The method of claim 74 comprising determining expression level of GZMM, wherein the expression level of GZMM in the sample is higher than a reference expression level of GZMM.

81. The method of claim 75 comprising determining expression levels of KIR2DS2 and KIR2DL2, wherein the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample is higher than a reference ratio.

82. The method of claim 75 comprising determining expression levels of KIR2DS5 and KIR2DL5, wherein the ratio of the expression level of KIR2DS5 to the expression level of KIR2DL5 in the sample is higher than a reference ratio.

83. The method of any one of claims 74 to 82, wherein said sample is a blood sample or a bone marrow sample.

84. The method of any one of claims 74 to 82, wherein said sample is PBMC.

85. The method of any one of claims 74 to 82, wherein said sample is enriched NK cells.

86. The method of any one of claims 74 to 85, wherein said expression level of a biomarker is measured by determining the protein level of said biomarker.

~~87. The method of claim 86 wherein the protein level of said biomarker is determined using a immunohistochemistry (IHC) approach, an immunoblotting assay, flow cytometry (FACS), or ELISA.~~

~~88. The method of claim 86 comprising contacting the sample with an antibody that immunospecifically binds to said biomarker protein.~~

~~89. The method of any one of claims 74 to 85, wherein said expression level of a biomarker is measured by determining the RNA level of said biomarker.~~

~~90. The method of claim 89, wherein the mRNA level of said biomarker is measured using qPCR, RT-PCR, RNA-seq, microarray analysis, SAGE, MassARRAY technique, or FISH.~~

~~91. The method of any one of claims 62 to 90, wherein said cancer is acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), chronic myelomonocytic leukemia (CMML), natural killer cell lymphoma (NK lymphoma), natural killer cell leukemia (NK leukemia), cutaneous T-Cell lymphoma (CTCL), peripheral T-cell lymphoma (PTCL), chronic myeloid leukemia (CML) or a solid tumor.~~

~~92. The method of claim 91, wherein said cancer is AML.~~

~~93. The method of claim 92, wherein said subject is post-remission induction or post-transplantation.~~

~~94. The method of claim 92, wherein said subject is over age 60 or otherwise unfit for remission induction.~~

~~95. The method of claim 91, wherein said cancer is MDS.~~

~~96. The method of claim 95, wherein said MDS is low risk MDS, intermediate risk MDS, or high risk MDS.~~

~~97. The method of claim 95, wherein said MDS is lower risk MDS.~~

~~98. The method of claim 91, wherein said cancer is CMML.~~

~~99. The method of claim 98, wherein said CMML is low risk CMML or intermediate risk CMML.~~

~~100. The method of claim 98, wherein said CMML is myelodysplastic CMML or myeloproliferative CMML.~~

~~101. The method of claim 98, wherein said CMML is NRAS/KRAS wild type CMML.~~

~~102. The method of claim 91, wherein said cancer is NK lymphoma or NK leukemia.~~

~~103. The method of claim 91, wherein said cancer is CTCL or PTCL.~~

~~104. The method of claim 91, wherein said cancer is a solid tumor selected from the group consisting of hepatocelluar carcinoma, head and neck cancer, salivary gland tumor, thyroid tumor, breast cancer, melanoma, gastric cancer, pancreatic cancer, and lung cancer.~~

~~105. A method of treating MDS in a subject comprising~~

~~(a) KIR typing said subject, wherein said subject is a carrier of KIR2DS2 or KIR2DS5, and~~

~~(b) administering a therapeutically effective amount of tipifarnib to said subject.~~

~~106. The method of claim 105 further comprising HLA typing said subject, wherein said subject is a carrier of HLA-C2.~~

~~107. The method of claim 106, wherein said subject is a carrier of KIR2DS2 and HLA-C2.~~

~~108. The method of claim 106 or 107 wherein said carrier of HLA-C2 is homozygous for HLA-C2.~~

~~109. A method of treating MDS in a subject comprising~~
~~(a) determining expression level of a biomarker selected from the group consisting of KIR2DS2, KIR2DL2, KIR2DS5, KIR2DL5, and GZMM in a sample from said subject, wherein~~

~~(i) the expression level of KIR2DS2 in the sample is higher than a reference expression level of KIR2DS2;~~

~~(ii) the expression level of KIR2DL2 in the sample is lower than a reference expression level of KIR2DL2;~~

(iii) the expression level of KIR2DS5 in the sample is higher than a reference expression level of KIR2DS5;

(iv) the expression level of KIR2DL5 in the sample is lower than a reference expression level of KIR2DL5; or

(v) the expression level of GZMM in the sample is higher than a reference expression level of GZMM; and

(b) administering a therapeutically effective amount of tipifarnib to said subject.

110. A method of treating MDS in a subject comprising

(a) determining expression levels of KIR2DS2 and KIR2DL2, or KIR2DS5 and KIR2DL5 in a sample from said subject, wherein

(i) the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample is higher than a reference ratio; or

(ii) the ratio of the expression level of KIR2DS5 to the expression level of KIR2DL5 in the sample is higher than a reference ratio; and

(b) administering a therapeutically effective amount of tipifarnib to said subject.

111. A method of selecting a cancer patient for an FTI treatment comprising

(a) KIR typing said cancer patient, wherein said cancer patient is a carrier of KIR2DS2 or KIR2DS5, and

(b) administering a therapeutically effective amount of an FTI to said cancer patient

112. The method of claim 111 further comprising HLA typing said subject, wherein said subject is a carrier of HLA-C2.

113. The method of claim 112, wherein said subject is a carrier of KIR2DS2 and HLA-C2.

114. The method of claim 112 or 113 wherein said carrier of HLA-C2 is homozygous for HLA-C2.

115. A method of selecting a cancer patient for an FTI treatment comprising

(a) determining expression level of a biomarker selected from the group consisting of KIR2DS2, KIR2DL2, KIR2DS5, KIR2DL5, and GZMM in a sample from said subject, wherein

(i) the expression level of KIR2DS2 in the sample is higher than a reference expression level of KIR2DS2;

(ii) the expression level of KIR2DL2 in the sample is lower than a reference expression level of KIR2DL2;

(iii) the expression level of KIR2DS5 in the sample is higher than a reference expression level of KIR2DS5;

(iv) the expression level of KIR2DL5 in the sample is lower than a reference expression level of KIR2DL5; or

(v) the expression level of GZMM in the sample is higher than a reference expression level of GZMM; and

(b) administering a therapeutically effective amount of an FTI to said subject.

116. A method of selecting a cancer patient for an FTI treatment comprising (a) determining expression levels of KIR2DS2 and KIR2DL2, or KIR2DS5 and KIR2DL5 in a sample from said subject, wherein

(i) the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample is higher than a reference ratio; or

(ii) the ratio of the expression level of KIR2DS5 to the expression level of KIR2DL5 in the sample is higher than a reference ratio; and

(b) administering a therapeutically effective amount of an FTI to said subject.

117. A method of inhibiting activity of NK cell in a subject comprising (a) KIR typing said subject, wherein said subject is a carrier of KIR2DS2 or KIR2DS5, and (b) administering a therapeutically effective amount of an FTI to said subject.

118. The method of claim 117 further comprising HLA typing said subject, wherein said subject is a carrier of HLA-C2.

119. A method of inhibiting activity of NK cell in a subject comprising (a) determining expression level of a biomarker selected from the group consisting of KIR2DS2, KIR2DL2, KIR2DS5, KIR2DL5, and GZMM in a sample from said subject, wherein

(i) the expression level of KIR2DS2 in the sample is higher than a reference expression level of KIR2DS2;

(ii) the expression level of KIR2DL2 in the sample is lower than a reference expression level of KIR2DL2;

(iii) the expression level of KIR2DS5 in the sample is higher than a reference expression level of KIR2DS5;

(iv) the expression level of KIR2DL5 in the sample is lower than a reference expression level of KIR2DL5; or

(v) the expression level of GZMM in the sample is higher than a reference expression level of GZMM; and

(b) administering a therapeutically effective amount of an FTI to said subject.

120. A method of inhibiting activity of NK cell in a subject comprising (a) determining expression levels of KIR2DS2 and KIR2DL2, or KIR2DS5 and KIR2DL5 in a sample from said subject, wherein

(i) the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample from said subject is higher than a reference ratio; or

(ii) the ratio of the expression level of KIR2DS5 to the expression level of KIR2DL5 in the sample from said subject is higher than a reference ratio; and (b) administering a therapeutically effective amount of an FTI to said subject.

121. The method of any one of claims 1 to 120, wherein the FTI is selected from the group consisting of tipifarnib, arglabin, perrilyl alcohol, lonafarnib (SCH-66336), L778123, L739749, FTI-277, L744832, CP-609,754, R208176, AZD3409, and BMS-214662.

12. The use of any one of claims 1-9, wherein the FTI contained in the medicament is suitable for administering for a period of one to seven days; or

wherein the FTI is suitable for administering on days 1 to 7 and 15 to 21 of a 28-day treatment cycle; or

wherein the FTI is suitable for administering for at least 3 cycles or for at least 6 cycles.

13. The use of any one of claims 1-9, wherein the FTI is suitable for administration at a dose of 300 mg twice a day for 3 out of 4 weeks in repeated 4 week cycles; or

wherein the FTI is suitable for administration at a dose of 600 mg twice a day on days 1 to 7 and 15 to 21 of a 28-day treatment cycle; or

wherein the FTI is suitable for administration at a dose of 900 mg twice a day on days 1 to 7 and 15 to 21 of a 28-day treatment cycle.

14. The use of any one of claims 1-9, wherein the FTI is suitable for administration further comprising radiation therapy; and

wherein the FTI is suitable for administration before, during, or after irradiation.

15. The use of any one of claims 1-9, wherein the FTI is suitable for administration further comprising a therapeutically effective amount of a second active agent or a supportive care therapy.

16. The use of claim 15, wherein the second active agent is selected from the group consisting of an anti-EGFR antibody, cisplatin, carboplatin, a taxane, gemcitabine, and methotrexate; or wherein the second active agent is an anti-PD1 antibody or an anti-PDL1 antibody.

~~122~~17. The ~~method~~use of any one of claims 1-9~~claim 121,~~ wherein the FTI is tipifarnib.

~~123. The method of any one of claims 1 to 122, wherein the FTI is administered orally, parenterally, rectally, or topically.~~

~~124~~18.. The ~~method~~ use of ~~any one of claims 1 to 123~~claim 17, wherein the amount of tipifarnib contained in the medicament is suitable for administering~~FTI is administered~~ at a dose of 1-1000 mg/kg body weight.

~~125~~19. The ~~method of any one of claims 1 to 124~~ use of claim 17, wherein the ~~FTI~~ amount of tipifarnib contained in the medicament is suitable for ~~is administered~~administering twice a ~~day~~day.

~~126~~20. The use of claim 17~~method of claim 125~~, wherein the ~~FTI~~ amount of tipifarnib contained in the medicament is suitable for administering ~~is administered~~ at a dose of ~~200-1200~~ 300 mg twice a day, or ~~.~~

~~127. The method of claim 125, wherein the FTI is administered~~ at a dose of 600 mg twice a day~~., or~~

~~128. The method of claim 125, wherein the FTI is administered~~ at a dose of 900 mg twice a day.

~~129~~21. The ~~method of any one of claims 1 to 128~~ use of claim 17, wherein the amount of tipifarnib contained in the medicament is suitable for administering ~~the FTI is administered~~ for a period ~~of~~ of one to seven days.

~~130. The method of any one of claims 1 to 129, wherein the FTI is administered in alternative weeks.~~

~~131~~22. The use of claim 17,~~method of any one of claims 1 to 130~~, wherein the amount of tipifarnib contained in the medicament is suitable for administering ~~the FTI is administered~~ on days 1- 7 and 15-21 of a 28-day treatment cycle~~.~~, optionally at doses up to 1600 mg twice a day.

23. The use of claim 17, wherein the amount of tipifarnib contained in the medicament is suitable for administering at a dose of 600 mg twice a day on days 1-7 and 15-21 of a 28-day treatment cycle.

24. The use of claim 17, wherein the amount of tipifarnib contained in the medicament is suitable for administering at a dose of 900 mg twice a day on days 1-7 and 15-21 of a 28-day treatment cycle.

25. The use of claim 17, wherein the amount of tipifarnib contained in the medicament is suitable for administering at a dose of 300 mg twice a day for 3 of 4 weeks in a repeated 4 week cycles, or at a dose of 300 mg twice a day on days 1-7 and 15-21 of a 28-day treatment cycle.

~~1322~~26. The ~~method of claim 131~~ use of claim 22, wherein the amount of tipifarnib contained in the medicament is suitable for administering ~~the FTI is administered~~ for at least 3 cycles~~.~~

~~133. The method of claim 131, wherein the FTI is administered~~ or for at least 6 cycles.

~~134. The method of claim 131, wherein said treatment cycle continues for up to 12 months.~~

~~135. The method of claim 132, wherein tipifarnib is administered orally at a dose of 900 mg twice a day on days 1-7 and 15-21 of a 28-day treatment cycle.~~

~~1362~~7. The ~~method of any one of claims 1 to 135~~use of claim 17, wherein the medicament is suitable for administering ~~the FTI is administered~~ before, ~~,~~ during, or after irradiation.

~~1372~~8. The ~~method of any one of claims 1 to 135~~use of claim 17, further ~~comprising administering~~ in combination with a therapeutically effective amount of a second active agent or a support care therapy.

~~1382~~9. The ~~method of claim 137~~use of claim 28, wherein ~~said~~ the second active agent is selected from the group consisting of a chemotherapeutic agent, a DNA-hypomethylating agent, a therapeutic antibody that specifically binds to a cancer antigen, a hematopoietic growth factor, a cytokine, ~~anti-cancer agent,~~ an antibiotic, a cox-2 inhibitor, an immunomodulatory agent, an anti-thymocyte globulin, an immunosuppressive agent, ~~,~~ and a corticosteroid or a pharmacological~~ly~~ derivative thereof ~~.~~ or

~~139. The method of claim 137,~~ wherein ~~said~~the second active agent is an anti-PD1 antibody or an ~~,~~anti-PDL1 antibody.

~~140. A kit for predicting the responsiveness of a cancer patient to an FTI treatment comprising at least one agent for KIR typing said cancer patient, and an ancillary agent, wherein said cancer patient is predicted to be responsive to the FTI treatment if said cancer patient is a carrier of KIR2DS2 or KIR2DS5.~~

~~141. The kit of claim 140 further comprising an agent for HLA typing said cancer patient, wherein said cancer patient is a carrier of HLA-C2.~~

142. A kit for predicting the responsiveness of a cancer patient to an FTI treatment comprising at least one agent for determining expression of at least one biomarker in a sample from the cancer patient, and an ancillary agent, wherein said biomarker is selected from the group consisting of KIR2DS2, KIR2DL2, KIR2DS5, KIR2DL5, and GZMM; wherein said cancer patient is predicted to be responsive to the FTI treatment if

(i) the expression level of KIR2DS2 in the sample is higher than a reference expression level of KIR2DS2;

(ii) the expression level of KIR2DL2 in the sample is lower than a reference expression level of KIR2DL2;

(iii) the expression level of KIR2DS5 in the sample is higher than a reference expression level of KIR2DS5;

(iv) the expression level of KIR2DL5 in the sample is lower than a reference expression level of KIR2DL5;

(v) the expression level of GZMM in the sample is higher than a reference expression level of GZMM;

(vi) the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample is higher than a reference ratio; or

(vii) the ratio of the expression level of KIR2DS5 to the expression level of KIR2DL5 in the sample is higher than a reference ratio.

143. A kit for predicting the responsiveness of a cancer patient to an FTI treatment comprising one or more agent for determining expression level of KIR2DS2 and KIR2DL2 in a sample from the cancer patient, and an ancillary agent; wherein said patient is predicted to be responsive to the FTI treatment if

i) the expression level of KIR2DS2 in the sample of said patient is higher than a reference expression level of KIR2DS2;

(ii) the expression level of KIR2DL2 in the sample from said patient is lower than a reference expression level of KIR2DL2; or

~~(iii) the ratio of the expression level of KIR2DS2 to the expression level of KIR2DL2 in the sample from said patient is higher than a reference ratio.~~

~~144. The kit of any one of claims 140 to 143 further comprising a label indicating the kit is used for predicting the responsiveness of a cancer patient to an FTI treatment.~~

~~145. The kit of any one of claims 140 to 143 wherein said patient is a MDS patient, and said FTI is tipifarnib.~~