CLAIMS

We claim:

1. Use of a composition in the manufacture of a medicament for a method of treating a squamous cell carcinoma (SCC) in a subject, the composition comprising a farnesyltransferase inhibitor (FTI), wherein the medicament is to be administered to said subject that has H-Ras overexpressing SCC.

2. The use of claim 1, wherein said subject has a H-Ras expression that is at least 2 fold, at least 3 fold, at least 4 fold, at least 5 fold, at least 10 fold, at least 15 fold, or at least 20 fold greater than a reference level.

3. The use of claim 1 or claim 2, wherein the reference level is the median expression level of H-Ras in a population of healthy subjects.

4. The use of claim 1 or claim 2, wherein the reference level is the median expression level of H-Ras in a population of subjects having SCC.

5. Use of a composition in the manufacture of a medicament for a method of treating a SCC in a subject, the composition comprising a FTI, wherein said subject has a higher ratio of H-Ras expression to K-Ras expression than a reference ratio.

6. Use of a composition in the manufacture of a medicament for a method of treating a SCC in a subject, the composition comprising a FTI, wherein said subject has a higher ratio of H-Ras expression to N-Ras expression than a reference ratio.

7. Use of a composition in the manufacture of a medicament for a method of treating a SCC in a subject, the composition comprising a FTI, wherein said subject has a higher ratio of H-Ras expression to the combined expression of K-Ras and N-Ras than a reference ratio.

8. The use of any one of claims 5 to 7, wherein the reference ratio is the median ratio in a population of healthy subjects.

9. The use of any one of claims 5 to 7, wherein the reference level is the median ratio in a population of subjects having SCC.

10. The use of any one of claims 5 to 7, wherein the reference ratio is 1/10, 1/9, 1/8, 1/7, 1/6, 1/5, 1/4, 1/3, 1/2, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

11. The use of any one of claims 1 to 10, wherein said SCC has an H-Ras mutation.

12. The use of claim 11, wherein said H-Ras mutation is or comprises a modification in a codon that encodes an amino acid substitution at a specific position selected from a group consisting of G12, G13, Q61, Q22, K117, A146, and any combination thereof, in the corresponding mutant H-Ras protein.

13. The use of any one of claims 1 to 12, wherein the SCC is head and neck SCC (HNSCC), lung SCC (LSCC), thyroid SCC (TSCC), esophagus SCC (ESCC), bladder SCC (BSCC), or urothelial carcinoma (UC).

14. The use of claim 13, wherein the SCC is HNSCC.

15. The use of claim 14, wherein said HNSCC is HNSCC of the trachea, HNSCC of the maxilla, or HNSCC of the oral cavity.

16. The use of any one of claims 1-15, wherein said SCC is human papillomavirus (HPV)-negative.

17. The use of any one of claims 1-15, wherein said SCC is at an advanced stage or metastatic.

18. The use of any one of claims 1-15, wherein said SCC is relapsed.

19. The use of any one of claims 1-15, wherein said SCC is refractory.

20. The use of any one of claims 1-15 or 16-19, wherein the H-Ras expression level in a sample from said subject is analyzed before administration of the medicament to the subject.

21. The use of claim 20, wherein the K-Ras expression level, N-Ras expression level, or both in the sample are further analyzed.

22. The use of claim 20 or 21, wherein the protein level of H-Ras, K-Ras, N-Ras, or any combination thereof are measured.

23. The use of claim 22, wherein the protein level is determined using a immunohistochemistry (IHC) approach, an immunoblotting assay, flow cytometry (FACS), or ELISA.

24. The use of claim 20 or 21, wherein the mRNA level of H-Ras, K-Ras, N-Ras, or any combination thereof are measured.

25. The use of claim 24, wherein the mRNA level is measured using qPCR, RT-PCR, RNA-seq, microarray analysis, SAGE, MassARRAY technique, or FISH.

26. The use of any one of claims 20 to 25, wherein the mutation status of H-Ras in the sample is further determined.

27. The use of any one of claims 20 to 26, wherein said sample is a tissue biopsy, a tumor biopsy, or isolated cells.

28. The use of any one of claims 1-15 or 16 to 27-, wherein the FTI is selected from the group consisting of tipifarnib, lonafarnib, arglabin, perrilyl alcohol, L778123, L739749, FTI-277, L744832, CP-609,754, R208176, AZD3409, and BMS-214662.

29. The use of claim 28, wherein the FTI is tipifarnib.

30. The use of claim 29, wherein tipifarnib is to be administered at a dose of 0.05-500 mg/kg body weight.

31. The use of claim 29, wherein tipifarnib is to be administered twice a day.

32. The use of claim 29, wherein tipifarnib is to be administered at a dose of 100-1200 mg twice a day.

33. The use of claim 29, wherein the tipifarnib is to be administered at a dose of 100 mg, 200 mg, 300 mg, 400 mg, 600 mg, 900 mg or 1200 mg twice a day.

34. The use of claim 29, wherein the tipifarnib is to be administered on days 1-7 and 15-21 of a 28-day treatment cycle, days 1-21 of a 28-day treatment cycle, or days 1-7 of a 28-day treatment cycle.

35. The use of claim 34, wherein tipifarnib is to be administered for at least 1 cycle.

36. The use of claim 35, wherein tipifarnib is to be administered for at least 3 cycles, 6 cycles, 9 cycles, or 12 cycles.

37. The use of any one of claims 29, 30-34, or 35-36, wherein tipifarnib is to be administered before, during, or after radiation.

38. The use of any one of claims 1-15, 16-17, 28-29, 30-34 or 35-37, wherein the medicament is to be administered with a second active agent.

39. The use of claim 38, wherein tipifarnib is to be administered before, during, or after the administration of said second active agent.

40. The use of claim 38 to 39, wherein said second active agent is selected from the group consisting of a DNA-hypomethylating agent, an alkylating agent, a topoisomerase inhibitor, a therapeutic antibody that specifically binds to a cancer antigen, a hematopoietic growth factor, a cytokine, an antibiotic, a cox-2 inhibitor, a CDK inhibitor, a PI3K-α inhibitor, an AKT inhibitor an MTOR 1/2 inhibitor, an immunomodulatory agent, an anti-thymocyte globulin, an immunosuppressive agent, and a corticosteroid or a pharmacological derivative thereof.

41. The use of claim 38 to 39, wherein said second active agent is an EGFR inhibitor.

42. The use of claim 41, wherein said EGFR inhibitor is cetuximab.

43. The use of claim 38 to 39, wherein said second active agent is an alkylating agent.

44. The use of claim 43, wherein said alkylating agent is cisplatin.

45. The use of claim 38 to 39, wherein said second active agent is a CDK inhibitor.

46. The use of claim 45, wherein said CDK inhibitor is palbociclib.

47. The use of claim 38 to 39, wherein said second active agent is a PI3K-α inhibitor.

48. The use of claim 47, wherein said PI3K-α inhibitor is BYL719.

49. The use of claim 38 to 39, wherein said second active agent is an AKT inhibitor.

50. The use of claim 49, wherein said AKT inhibitor is GSK2141795.

51. The use of claim 38 to 39, wherein said second active agent is an MTOR 1/2 inhibitor.

52. The use of claim 51, wherein said MTOR 1/2 inhibitor is INK-128.

53. The use of claim 38 to 39, wherein said second active agent is an anti-PD1 antibody, an anti-PDL1 antibody, or an anti-CTLA-4 antibody.

54. The use of any one of claims 1-15, 16-27, 28-29, 30-34, or 35-37, wherein the medicament is to be administered with a support care therapy.