CLAIMS

We claim:

1. Use of tipifarnib in the manufacture of a medicament that is to be administered in combination with a therapeutically effective amount of PI3K-α inhibitor BYL719 for a method of treating a head and neck squamous cell carcinoma (HNSCC) in a subject, wherein the HNSCC is a wild-type H-Ras-overexpressing HNSCC.

2. The use of claim 1, wherein the HNSCC has wild-type H-Ras overexpression that is greater than a median expression level of wild-type H-Ras in corresponding tissue in a population of healthy subjects.

3. The use of claim 1, wherein the HNSCC has wild-type H-Ras overexpression that is greater than a median expression level of wild-type H-Ras in corresponding tissue in a population of subjects having HNSCC.

4. The use of any one of claims 1-3, wherein the HNSCC expresses wild-type PI3K-α protein.

5. The use of any one of claims 1-4, wherein the HNSCC has amplified wild-type PIK3CA gene.

6. The use of any one of claims 1-5, wherein the HNSCC expresses mutant PI3K-α protein.

7. The use of any one of claims 1-6, wherein the HNSCC has a PIK3CA gene mutation.

8. The use of claim 7, wherein the PIK3CA gene mutation comprises a modification in a codon that encodes an amino acid substitution at a specific position selected from a group consisting of G118, E545, and a combination thereof, in the corresponding wild-type PI3K-α protein.

9. The use of any one of claims 1-8, wherein the HNSCC has amplified mutant PI3K-α protein.

10. The use of any one of claims 1-9, wherein said HNSCC is HNSCC of the trachea, HNSCC of the maxilla, or HNSCC of the oral cavity.

11. The use of any one of claims 1-10, wherein said HNSCC is human papillomavirus (HPV)-negative.

12. The use of any one of claims 1-11, wherein said HNSCC is at an advanced stage, relapsed, or refractory.

13. The use of any one of claims 1-12, wherein said HNSCC is metastatic.

14.. The use of any one of claims 1-13, wherein the tipifarnib is to be administered twice a day.

15. The use of any one of claims 1-14, wherein the tipifarnib is to be administered at a dose of 100-1200 mg twice a day.

16. The use of any one of claims 1-15, 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.

17. The use of any one of claims 1-16, 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.

18. The use of claim 17, wherein the tipifarnib is to be administered for at least 1 cycle.

19. The use of claim 18, wherein the tipifarnib is to be administered for at least 3 cycles, 6 cycles, 9 cycles, or 12 cycles.

20. The use of any one of claims 1-19, wherein the tipifarnib is to be administered before, during, or after radiation.

21. The use of any one of claims 1-20, wherein the tipifarnib is to be administered before, during, or after the administration of the PI3K-α inhibitor BYL719.

22. The use of any one of claims 1-21, wherein the medicament is to be administered with a support care therapy.