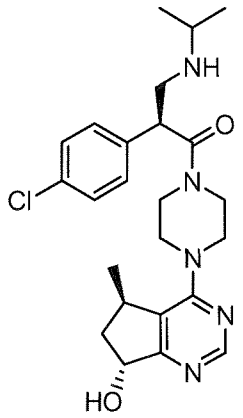
We claim:

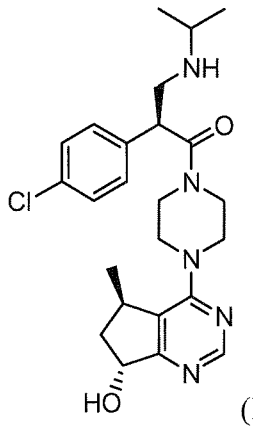
1. A combination of a compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof; and an agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof, for the therapeutic treatment of a hyperproliferative disorder.

2. Use of a compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof; and an agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof, for the therapeutic treatment of a hyperproliferative disorder.

3. The use of claim 2, wherein the hyperproliferative disorder is cancer.

4. The use of claim 3, wherein the cancer is associated with PTEN mutation.

5. The use of claim 3, wherein the cancer is associated with AKT mutation, overexpression or amplification.

6. The use of claim 3, wherein the cancer is associated with PI3K mutation.

7. The use of claim 3, wherein the cancer is associated with Her2/ErbB2 amplification.

8. The use of any one of claims 3-7, wherein cancer is selected from, mesothelioma, endometrial, pancreatic, breast, lung, ovarian, prostate, melanoma, gastric, colon, renal, head and neck, and glioma.

9. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973.

10. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with PD-0325901.

11. The use of any one of claims 2-10, wherein the compound of formula I or the salt thereof is to be administered simultaneously with the one or more agents.

12. The use of any one of claims 2-10, wherein the compound of formula I or the salt and the one or more agents are to be administered sequentially.

13. The use of any one of claims 2-10, wherein administration of the one or more agents begins about 1 to about 10 days before administration of the combination.

14. The use of any one of claims 2-10, wherein administration of the compound of formula I or the salt thereof begins about 1 to about 10 days before administration of the combination.

15. The use of any one of claims 2-10, wherein administration of the compound of formula I or the salt thereof and administration of the one or more agents begins on the same

day.

16. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is pancreatic.

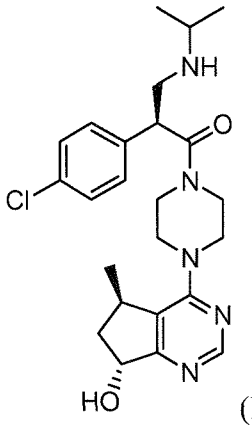
17. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is non-small cell lung cancer.

18. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is breast.

19. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is colon.

20. The use of any one of claims 2-8, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is melanoma.

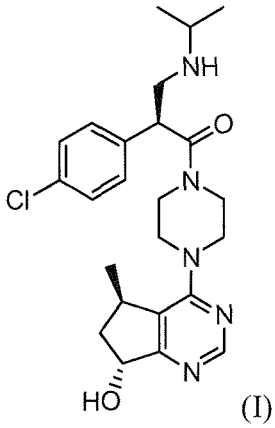
21. The combination of a) a compound of formula I



(I)

or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof for treating a hyperproliferative disorder.

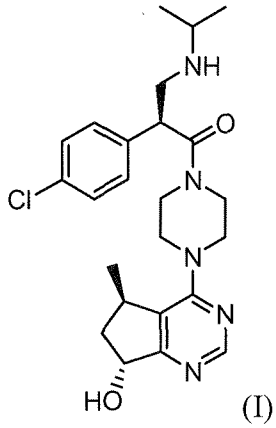
22. The combination of a) a compound of formula I



(I)

or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof for treating a disease or condition modulated by AKT kinase.

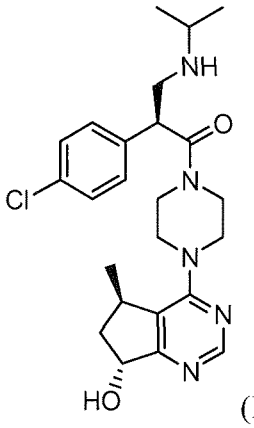
23. The use of the combination of a compound of formula I



(I)

or a pharmaceutically acceptable salt thereof and GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a hyperproliferative disorder in a mammal.

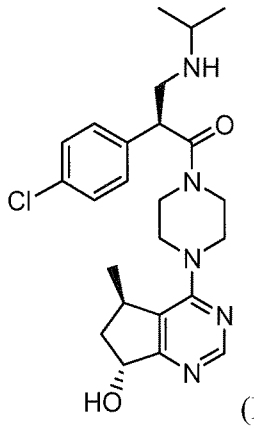
24. A kit comprising a compound of formula I



(I)

or a pharmaceutically acceptable salt thereof, a container, and a package insert or label indicating the administration of the compound of formula I with one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof for treating a hyperproliferative disorder.

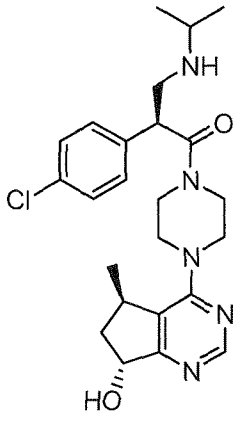
25. A product comprising a compound having formula I



(I)

or a pharmaceutically acceptable salt thereof, and one or more agents selected GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof; as a combined preparation for separate, simultaneous or sequential use in the treatment of a hyperproliferative disorder.

26. Use of a combination of a compound of formula I:

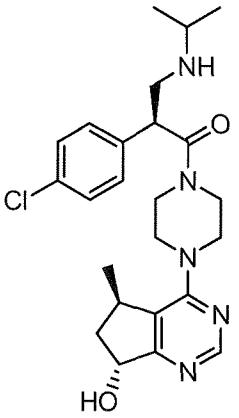


(I)

or a pharmaceutically acceptable salt thereof; and another agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a hyperproliferative disorder in a mammal.

ABSTRACT

The invention provides combinations comprising a) compound of formula I:

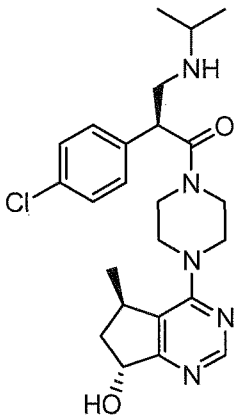


(I)

or a pharmaceutically acceptable salt thereof; and another agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof. The combinations are particularly useful for treating hyperproliferative disorders, such as cancer.

We claim:

1. A combination of a compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof; and an agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof, for the prophylactic or therapeutic treatment of a hyperproliferative disorder.

2. The combination of claim 1, wherein the hyperproliferative disorder is cancer.

3. The combination of claim 2, wherein the cancer is associated with PTEN mutation.

4. The combination of claim 2, wherein the cancer is associated with AKT mutation, overexpression or amplification.

5. The combination of claim 2, wherein the cancer is associated with PI3K mutation.

6. The combination of claim 2, wherein the cancer is associated with Her2/ErbB2 amplification.

7. The combination of any one of claims 2-6, wherein cancer is selected from, mesothelioma, endometrial, pancreatic, breast, lung, ovarian, prostate, melanoma, gastric, colon, renal, head and neck, and giloma.

8. The combination of any one of claims 1-7, wherein a compound of formula I, or a

pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973.

9. The combination of any one of claims 1-7, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with PD-0325901.

10. The combination of any one of claims 1-9, wherein the compound of formula I or the salt thereof is to be administered simultaneously with the one or more agents.

11. The combination of any one of claims 1-9, wherein the compound of formula I or the salt and the one or more agents are to be administered sequentially.

12. The combination of any one of claims 1-9, wherein administration of the one or more agents begins about 1 to about 10 days before administration of the combination.

13. The combination of any one of claims 1-9, wherein administration of the compound of formula I or the salt thereof begins about 1 to about 10 days before administration of the combination.

14. The combination of any one of claims 1-9, wherein administration of the compound of formula I or the salt thereof and administration of the one or more agents begins on the same day.

15. The combination of any one of claims 1-7, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is pancreatic.

16. The combination of any one of claims 1-7, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is non-small cell lung cancer.

17. The combination of any one of claims 1-7, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is breast.

18. The combination of any one of claims 1-7, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is colon.

19. The combination of any one of claims 1-7, wherein a compound of formula I, or a pharmaceutically acceptable salt thereof, is to be administered in combination with GDC-0973, and the cancer is melanoma.

20. A compound of formula I or a pharmaceutically acceptable salt thereof, for therapeutic use for improving the quality of life of a patient treated for a hyperproliferative disorder with an agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof.

21. The combination of a) a compound of formula I or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof for treating a hyperproliferative disorder.

22. The combination of a) a compound of formula I or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof for treating a disease or condition modulated by AKT kinase.

23. The use of the combination of a compound of formula I or a pharmaceutically acceptable salt thereof and GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a hyperproliferative disorder in a mammal.

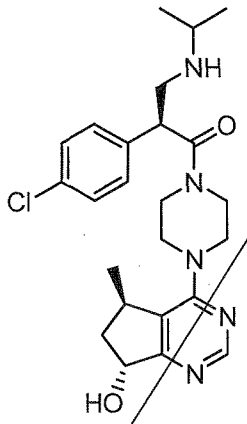
24. The use of the combination of a compound of formula I or a pharmaceutically acceptable salt thereof and GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof in preparation of a medicament for the treatment of a disease or condition modulated by AKT kinase in a mammal.

25. A kit comprising a compound of formula I or a pharmaceutically acceptable salt thereof, a container, and a package insert or label indicating the administration of the

compound of formula I with one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof for treating a hyperproliferative disorder.

26. A product comprising a compound having formula I or a pharmaceutically acceptable salt thereof, and one or more agents selected GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof; as a combined preparation for separate, simultaneous or sequential use in the treatment of a hyperproliferative disorder.

27. Use of a combination of a compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof; and another agent selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a hyperproliferative disorder in a mammal.

28. Use of a) a compound of formula I or a pharmaceutically acceptable salt thereof; and b) one or more agents selected from GDC-0973, PD-0325901, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition modulated by AKT kinase in a mammal.