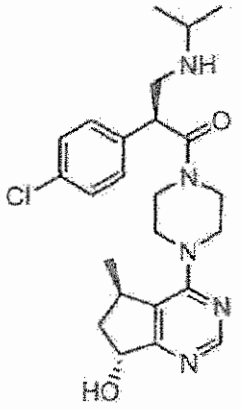
We claim:

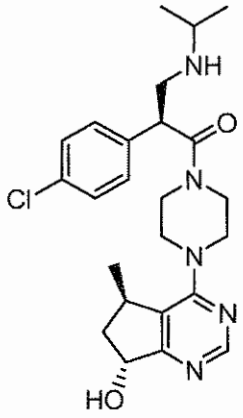
1. A combination of a) a compound of Formula Ia:



Ia,

or a pharmaceutically acceptable salt thereof, and b) vemurafenib or a pharmaceutically acceptable salt thereof for use in the therapeutic treatment of a hyperproliferative disorder.

2. The use of a compound of formula Ia



Ia

or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of cancer in a mammal, wherein vemurafenib or a pharmaceutically acceptable salt thereof is to be administered to the mammal.

3. The use of claim 2, wherein compound of formula Ia or the salt thereof is to be administered simultaneously with the vemurafenib or a pharmaceutically acceptable salt thereof.

4. The use of claim 2, wherein the compound of formula Ia or the salt thereof is to be administered sequentially with the vemurafenib or a pharmaceutically acceptable salt thereof.

5. The use of claim 2, wherein the compound of formula Ia or the salt thereof and the vemurafenib or a pharmaceutically acceptable salt thereof is to be administered separately.

6. The use of any one of claims 2-5 wherein the cancer comprises a BRAF V600E mutation.

7. The use of any one of claims 2-5 wherein the cancer is associated with high pAKT expression or activation levels.

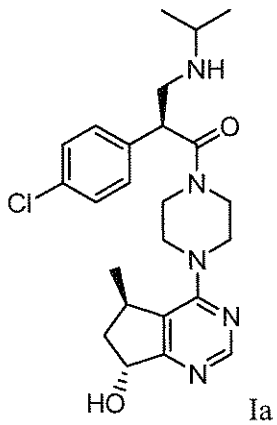
8. The use of any one of claims 2-7 wherein the cancer is lymphoma, colon, melanoma, thyroid or lung cancer.

9. The use of claim 8 wherein the cancer is resistant to vemurafenib single agent therapy.

10. The use of claim 9 wherein the cancer is metastatic or unresectable melanoma.

11. The use of any one of claims 1-10 wherein the combination provides asynergistic effect in treating the disorder.

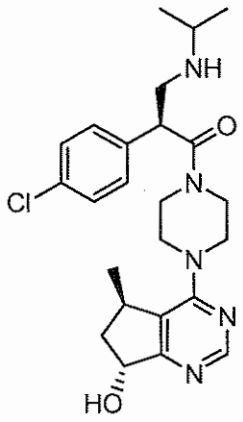
12. A compound of formula Ia



Ia

or a pharmaceutically acceptable salt thereof, for therapeutic use for improving the quality of life of a patient treated for cancer with vemurafenib or a pharmaceutically acceptable salt thereof.

13. Use of a) a compound of formula Ia

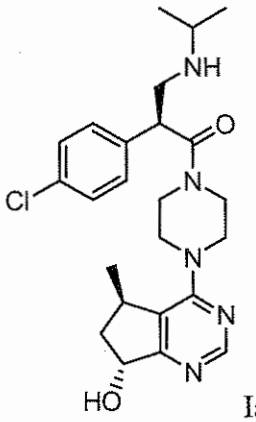


Ia

or a pharmaceutically acceptable salt thereof; and b) vemurafenib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a mammal, wherein the cancer is modulated by BRAF V600E mutation.

14. The use of claim 13, wherein the mammal is a patient, wherein said patient previously received vemurafenib single agent therapy.

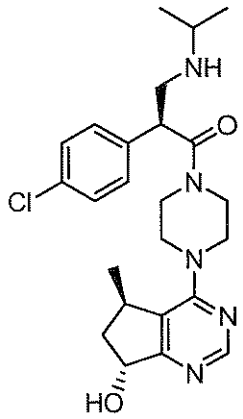
15. A kit comprising a compound of formula Ia



Ia

or a pharmaceutically acceptable salt thereof, a container, and a package insert or label indicating the administration of the compound of formula Ia with vemurafenib or a pharmaceutically acceptable salt thereof for treating cancer.

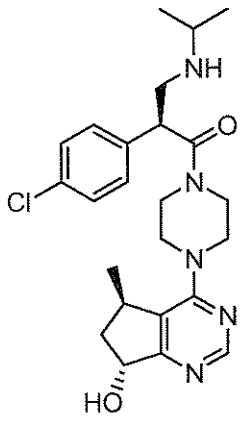
16. A product comprising a compound having formula Ia



Ia

or a pharmaceutically acceptable salt thereof, and vemurafenib or a pharmaceutically acceptable salt thereof as a combined preparation for separate, simultaneous or sequential use in the treatment of cancer.

17. A medicament for treating cancer in a mammal, wherein the cancer is modulated by BRAF V600E mutation comprising a) a compound of formula Ia



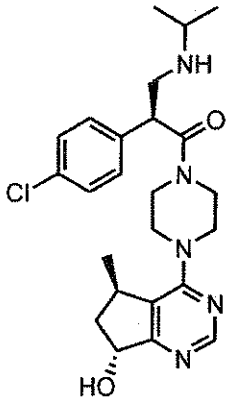
Ia,

or a pharmaceutically acceptable salt thereof; and b) vemurafenib or a pharmaceutically acceptable salt thereof.

18. The medicament of claim 17, wherein the mammal is a patient, wherein the patient previously received vemurafenib single agent therapy.

We claim:

1. A combination of a) a compound of Formula Ia:



Ia,

or a pharmaceutically acceptable salt thereof, and b) vemurafenib 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 comprises a BRAF V600E mutation.

4. The combination of claim 2 or 3 wherein the cancer is associated with high pAKT expression or activation levels.

5. The combination of any one of claims 2-4 wherein the cancer is lymphoma, colon, melanoma, thyroid or lung cancer.

6. The combination of claim 5 wherein the cancer is resistant to vemurafenib single agent therapy.

7. The combination of claim 6 wherein the cancer is metastatic or unresectable melanoma.

8. The combination of any one of claims 1-7 wherein the combination provides a

synergistic effect in treating the disorder.

9. The combination of any one of claims 1 -7 wherein the compound of formula la or the salt thereof is to be administered simultaneously with the vemurafenib or the salt thereof.

10. The combination of any one of claims 1-7 wherein the compound of formula la or the salt and the vemurafenib or the salt thereof are to be administered sequentially.

11. A compound of formula la or a pharmaceutically acceptable salt thereof as defined in claim 1, for therapeutic use for improving the quality of life of a patient treated for a hyperproliferative disorder with vemurafenib or a pharmaceutically acceptable salt thereof.

12. Use of a) a compound of formula la or a pharmaceutically acceptable salt thereof as defined in claim 1; and b) vemurafenib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a disease or condition modulated by BRAF V600E mutation and high pAKT levels in a mammal.

13. The use of claim 12, wherein the patient previously received vemurafenib single agent therapy.

14. The use of a compound of formula la or a pharmaceutically acceptable salt thereof as defined in claim 1 in the preparation of a medicament for the treatment of a hyperproliferative disorder in a mammal, wherein vemurafenib is to be administered to the mammal.

15. The use of a compound of formula la or a pharmaceutically acceptable salt thereof as defined in claim 1 in the preparation of a medicament for the treatment of a disease or condition modulated by AKT kinase in a mammal, wherein vemurafenib is to be administered to the mammal.