

CLAIMS

1. A drug combination for treating a neoplasm in a subject, comprising:
poziotinib or a pharmaceutically acceptable salt thereof; and
a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor.
2. The drug combination of claim 1, wherein the VEGFR2 inhibitor is Ramucirumab.
3. The drug combination of claim 1, wherein the poziotinib is in a monohydrochloride salt form.
4. A kit for treating a neoplasm in a subject, comprising:
poziotinib or a pharmaceutically acceptable salt thereof; and
a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor.
5. The kit of claim 4, wherein the VEGFR2 inhibitor is Ramucirumab.
6. The kit of claim 4, further comprising an educational information and direction of use.
7. ~~A method for treating a neoplasm in a subject, comprising administering a drug combination according to any one of claim 1 to claim 3 to the subject. Use of poziotinib or a pharmaceutically acceptable salt thereof and a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor in the manufacture of a medicament for combination therapy for treating a neoplasm in a subject, wherein the medicament is to be administered to a subject according to any one of claim 1 to claim 3.~~
8. Use of poziotinib or a pharmaceutically acceptable salt thereof in the manufacture of a first medicament and use of a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating a neoplasm in a subject, and wherein the medicament is to be administered to a subject according to any one of claim 1 to claim 3.
9. Use of poziotinib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in combinatorial therapy for treating a neoplasm in a subject, wherein said medicament is to be administered to a subject in combination with a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor, according to any one of claim 1 to claim 3.

8.10. The ~~method-use~~ of claims 7 to 9, wherein the neoplasm is selected from the group consisting of non-small cell lung cancer, breast cancer, stomach cancer, colon cancer, pancreatic cancer, prostate cancer, myeloma, head and neck cancer, ovarian cancer, esophageal cancer, and metastatic cell carcinoma.

9.11. The ~~method-use~~ of claims 7 to 9, wherein the VEGFR2 inhibitor in the drug combination is Ramucirumab.

10.12. The ~~method-use~~ of claims 7 to 9, wherein the subject expresses a mutation at exon 18, exon 19, exon 20, or exon 21.

11.13. The ~~method-use~~ of claims 7 to 9, further comprising determining the subject as having one or more HER2 exon 20 mutations.

12.14. The ~~method-use~~ of claims 7 to 9, further comprising determining the subject as having one or more EGFR exon 20 mutations selected from the group consisting of A775insV G776C, A775insYVMA, G776C V777insC, G776del insVV, G776del insVC, P780insGSP, Y772dupYVMA, V773M, G776delinsLC, V777L, V777insCG, G778dupGSP, P780insGSP, L786V.

13.15. The ~~method-use~~ of claims 7 to 9, further comprising determining the subject as having one or more EGFR exon 20 mutations selected from the group consisting of A763insFQEA, A767insASV, S768dupSVD, V769insASV, D770insSVD, D770insNPG, H773insNPH, N771del insGY, N771del insFH, N771dupNPH, A767insTLA, S768I, V769L, V769insGSV, D770del insGY, D770insG, D770insY H773Y, N771insHH, P772insDNP, H773insAH, H773insH, V774insHV, S784F, R776C, V774M, V769M, G796D, S784F, C775Y, S811F, T790M, V774A, D770A.

14.16. The ~~method-use~~ of claims 7 to 9, further comprising determining the subject as having one or more HER2 exon 21 mutations selected from the group consisting of a point mutation, insertion, and deletion of 1-18 nucleotides between amino acids 832-883.

15.17. The ~~method-use~~ of claims 7 to 9, further comprising determining the subject as having one or more HER2 exon 21 mutations are at one or more residues selected from the group consisting of V842, R868, and L869.

16.18. The ~~method-use~~ of claims 7 to 9, wherein the neoplasm is non-small cell lung carcinoma.

~~17.19.~~ The ~~method-use~~ of claims 7 to 9, wherein the neoplasm is a metastatic cancer.

~~18.20.~~ The ~~method-use~~ of claims 7 to 9, wherein the cancer is refractory to chemotherapy or radiotherapy, resistant to chemotherapy, or has relapsed.

~~19.21.~~ The ~~use method~~ of claims 7 to 9, wherein the subject has previously received one, two, three or more lines of therap for the neoplasm.

~~20.22.~~ The ~~use method~~ of claims 7 to 9, wherein the subject has not previously received treatment with a EGFR tyrosine kinase inhibitor.

~~21.23.~~ The ~~use method~~ of claims 7 to 9, wherein the subject has received prior treatment with an EGFR tyrosine kinase inhibitor.

~~22.24.~~ The ~~use method~~ of claims 7 to 9, wherein the administration and / or dosage of the drug combination is controlled to treat or prevent CNS metastases in the subject.

~~23.25. A method of treating or preventing CNS metastases in a subject, wherein the subject has been diagnosed to have a cancer comprising administering a drug combination according to any one of claim 1 to claim 3 to the subject~~Use of poziotinib or a pharmaceutically acceptable salt thereof and a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor in the manufacture of a medicament for combination therapy for treating or preventing CNS metastases in a subject, wherein the subject has been diagnosed to have a cancer, and wherein the medicament is to be administered to a subject according to any one of claim 1 to claim 3.

26. Use of poziotinib or a pharmaceutically acceptable salt thereof in the manufacture of a first medicament and use of a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating or preventing CNS metastases in a subject, wherein the subject has been diagnosed to have a cancer, and wherein the medicament is to be administered to a subject according to any one of claim 1 to claim 3.

27. Use of poziotinib or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in combinatorial therapy for treating or preventing CNS metastases in a subject, wherein the subject has been diagnosed to have a cancer, and wherein said medicament

is to be administered to a subject in combination with a vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor, according to any one of claim 1 to claim 3

24.28. The use method of claims 2325 to 27, wherein the cancer is non-small cell lung cancer (NSCLC).

25.29. The use method of claim 2325 to 27, wherein the subject has been determined to have CNS metastases.

26.30. The use method of claim 25 to 2723, wherein the subject has been determined to have no CNS metastases.

27.31. The use method of claim 25 to 2723, wherein the subject has previously received one, two, three or more lines of therap for the neoplasm.

28.32. The use method of claim 25 to 2723, wherein the subject has not previously received treatment with a EGFR tyrosine kinase inhibitor.