

CLAIMS

1. A method of treating a HER2 positive cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a combination therapy comprising tucatinib, trastuzumab and an oxaliplatin-based chemotherapy.
2. A method of treating cancer in a subject in need thereof, the method comprising:
 - (a) identifying the subject as having a HER2 positive cancer; and
 - (b) administering to the subject a therapeutically effective amount of a combination therapy comprising tucatinib, trastuzumab, and an oxaliplatin-based chemotherapy.
3. The method of any one of claims 1 or 2, wherein the oxaliplatin-based chemotherapy is oxaliplatin in combination with a compound selected from the group consisting of leucovorin (LV), fluorouracil, uracil-tegafur (UFT), irinotecan, and bevacizumab, or a combination thereof.
4. The method of any one of claims 1-3 wherein the oxaliplatin-based chemotherapy is administered as a regimen selected from the group consisting of FOLFOX4, mFOLFOX4, FOLFOX6, mFOLFOX6, mFOLFOX7, FOLFOXIRI, bFOL, PVIFOX, IROX, FUOX, FuFOX, CapeOx, XELOX, and CAPOX.
5. The method of any one of claims 1-4, wherein the oxaliplatin-based chemotherapy comprises oxaliplatin, leucovorin, and fluorouracil administered as an mFOLFOX7 regimen.
6. The method of any one of claims 1-5, wherein the HER2 positive cancer is selected from the group consisting of gastric adenocarcinoma, gastroesophageal junction (GEJ) adenocarcinoma, esophageal adenocarcinoma, colorectal carcinoma (CRC), cholangiocarcinoma, gallbladder carcinoma, gastric cancer, lung cancer, biliary cancers, bladder cancer, esophageal cancer, melanoma, ovarian cancer, liver cancer, prostate cancer, pancreatic cancer, small intestine cancer, non-small cell lung cancer, head and neck cancer, uterine cancer, cervical cancer, brain cancer, and breast cancer

7. The method of any one of claims 1-6, wherein the HER2 positive cancer is gastric adenocarcinoma.
8. The method of any one of claims 1-6, wherein the HER2 positive cancer is gastroesophageal junction (GEJ) adenocarcinoma.
9. The method of any one of claims 1-6, wherein the HER2 positive cancer is esophageal adenocarcinoma.
10. The method of any one of claims 1-6, wherein the HER2 positive cancer is colorectal carcinoma (CRC).
11. The method of any one of claims 1-6, wherein the HER2 positive cancer is cholangiocarcinoma.
12. The method of any one of claims 1-6, wherein the HER2 positive cancer is gallbladder carcinoma.
13. The method of any one of claims 1-12, wherein the HER2 positive cancer is unresectable or metastatic.
14. The method of any one of claims 1-13, wherein the subject has not been previously treated with tucatinib.
15. The method of any one of claims 1-14, wherein the subject has not been previously treated with trastuzumab.
16. The method of any one of claims 1-15, wherein the subject has not been previously treated with an oxaliplatin-based chemotherapy.

17. The method of any one of claims 1-16, wherein the subject is a candidate to receive an oxaliplatin-based chemotherapy.
18. The method of any one of claims 1-15, wherein the subject was previously treated or is currently being treated with an oxaliplatin-based chemotherapy.
19. The method of any one of claims 1-18, wherein the subject was previously treated with at least one anticancer therapy.
20. The method of claim 19, wherein the least one anticancer therapy is an anti-HER2 antibody or an anti-HER2 antibody-drug conjugate.
21. The method of claim 19, wherein the at least one anticancer therapy is selected from the group consisting of trastuzumab, trastuzumab and a taxane, pertuzumab, ado-trastuzumab (T-DM1), and combinations thereof.
22. The method of any one of claims 19-21, wherein the subject is refractory to the at least one anticancer therapy.
23. The method of any one of claims 19-22, wherein the subject developed a brain metastasis during the previous treatment with the at least one anticancer therapy.
24. The method of any one of claims 1-23, wherein the subject has not been treated with another anticancer therapy within the past 12 months.
25. The method of any one of claims 1-24, wherein the tucatinib is administered to the subject at a dose of about 100 mg to about 1000 mg.
26. The method of any one of claims 1-25, wherein the tucatinib is administered twice daily.

27. The method of any one of claims 1-26, wherein the tucatinib is administered to the subject orally.
28. The method of any one of claims 1-27, wherein the trastuzumab is administered to the subject at a dose of about 6 mg/kg.
29. The method of any one of claims 1-28, wherein the trastuzumab is administered to the subject at a dose of about 4 mg/kg.
30. A method for treating a HER2 positive cancer in a subject that has exhibited an adverse event after starting treatment with a combination therapy comprising tucatinib, trastuzumab, and an oxaliplatin-based chemotherapy at an initial dosage level, comprising administering to the subject the at least one component of the combination therapy at a reduced dosage level.
31. The method of claim 30, wherein the tucatinib is administered to the subject at a dose of about 100 mg to about 1000 mg.
32. The method of any one of claims 30 or 31, wherein the trastuzumab is administered to the subject at a dose of about 6 mg/kg.
33. The method of any one of claims 30 or 31, wherein the trastuzumab is administered to the subject at a dose of about 4 mg/kg.
34. A kit for treating or ameliorating the effects of a HER2 positive cancer in a subject, the kit comprising tucatinib, trastuzumab, and an oxaliplatin-based chemotherapy.
35. A method of treating a HER2 positive cancer in a subject in need thereof, the method comprising:
- (a) administering to the subject a therapeutically effective amount of a combination therapy comprising tucatinib, trastuzumab, and an oxaliplatin-based chemotherapy; and

(b) administering an effective amount of an anti-diarrheal agent.

36. A method of reducing the severity or incidents of diarrhea, or preventing diarrhea in a subject having a HER2 positive cancer and being treated with an effective amount of a combination therapy comprising tucatinib, trastuzumab, and an oxaliplatin-based chemotherapy, the method comprising administering an effective amount of an anti-diarrheal agent prophylactically.

37. A method of reducing the likelihood of a subject developing diarrhea, wherein the subject has a HER2 positive cancer and is being treated with an effective amount of a combination therapy comprising tucatinib, trastuzumab, and an oxaliplatin-based chemotherapy the method comprising administering an effective amount of an anti-diarrheal agent prophylactically.

38. The method of any one of claims 36-37, wherein the combination therapy and the anti-diarrheal agent are administered concurrently.

39. The method of any one of claims 36-37, wherein the anti-diarrheal agent is administered prior to administration of the combination therapy.

40. The method of any one of claims 36-39, wherein the subject is exhibiting symptoms of diarrhea.

41. The method of any one of claims 36-39, wherein the subject is not exhibiting symptoms of diarrhea.