elevated tumour PD-L1 levels. (Morgillo F, Della Corte CM, Fasano M, et al. Mechanisms of resistance to EGFR-targeted drugs: lung cancer. ESMO Open 2016;1: e000060)

[008] There is a significant medical need in the art for a satisfactory treatment of cancer driven by EGFR. In addition to the single-agent targeted therapies strategies outlined above in first line and for overcoming the non-responsiveness exhibited by resistant cancers, combination treatments may also provide promise.

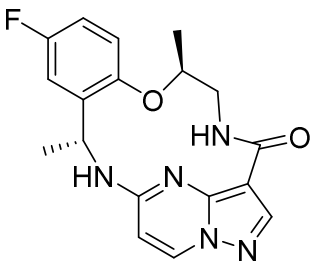
SUMMARY

[009] It has been discovered that the combination of an EGFR inhibitor and a triple inhibitor of FAK, SRC and JAK2 provides a robust response in cancers driven by EGFR.

[010] The disclosure provides a method for treating cancer in a host animal, the method comprising the step of administering to the host animal a therapeutically effective amount of a compound that inhibits FAK, SRC and JAK2, in combination with a therapeutically effective amount of at least one additional anti-cancer agent. In some examples, the additional anti-cancer agent is an EGFR inhibitor, or a pharmaceutically acceptable salt thereof.

[011] The disclosure provides a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer in a patient, in combination with a therapeutically effective amount of at least one additional anti-cancer agent. In some examples, the additional anti-cancer agent is an EGFR inhibitor, or a pharmaceutically acceptable salt thereof.

[011a] In one aspect, there is provided use of a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, and an EGFR inhibitor selected from afatinib, dacomitinib, gefitinib and osimeritinib, or a pharmaceutically acceptable salt thereof, in the manufacture of a combined preparation for simultaneous, separate or sequential administration in the treatment of cancer, wherein the compound that inhibits FAK, SRC and JAK2 is of the formula

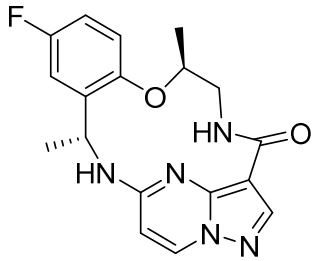


or a pharmaceutically acceptable salt thereof.

[012] In another example, there is provided use of a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament comprising a therapeutically effective amount of the compound, for treating cancer in a patient

in combination with a therapeutically effective amount of at least one additional anti-cancer agent. In some examples, the additional anti-cancer agent is an EGFR inhibitor, or a pharmaceutically acceptable salt thereof.

[012a] In another aspect, there is provided the use of a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament comprising a therapeutically effective amount of the compound, for treating cancer in a patient in combination with a therapeutically effective amount of an EGFR inhibitor selected from afatinib, dacomitinib, gefitinib and osimertinib, or a pharmaceutically acceptable salt thereof, wherein the compound that inhibits FAK, SRC and JAK2 is of the formula I or II

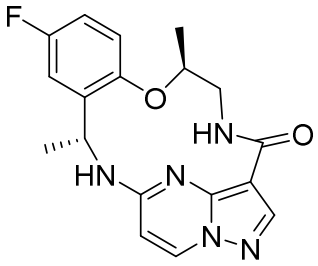


or a pharmaceutically acceptable salt thereof.

[013] In another example, there is provided a composition comprising a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, in a therapeutically effective amount, for use in the treatment of cancer in a patient, in combination with a therapeutically effective amount of at least one additional anti-cancer agent. In some examples, the additional anti-cancer agent is an EGFR inhibitor, or a pharmaceutically acceptable salt thereof.

WHAT IS CLAIMED IS:

1. Use of a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, and an EGFR inhibitor selected from afatinib, dacomitinib, gefitinib and osimertinib, or a pharmaceutically acceptable salt thereof, in the manufacture of a combined preparation to be simultaneously, separately or sequentially administered in the treatment of cancer, wherein the compound that inhibits FAK, SRC and JAK2 is of the formula



or a pharmaceutically acceptable salt thereof.

2. The use of any one claim 1, wherein the cancer is selected from the group consisting of ALCL, NSCLC, neuroblastoma, inflammatory myofibroblastic tumor, adult renal cell carcinoma, pediatric renal cell carcinoma, breast cancer, ER^+ breast cancer, triple negative breast, colonic adenocarcinoma, glioblastoma, glioblastoma multiforme, anaplastic thyroid cancer, cholangiocarcinoma, ovarian cancer, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma, epithelioid hemangioendothelioma, intrahepatic cholangiocarcinoma, thyroid cancer, spitzoid neoplasms, sarcoma, astrocytoma, brain lower grade glioma, secretory breast carcinoma, mammary analogue carcinoma, acute myeloid leukemia, congenital mesoblastic nephroma, congenital fibrosarcomas, Ph-like acute lymphoblastic leukemia, thyroid carcinoma, head and neck squamous cell carcinoma, pediatric glioma CML, prostate cancer, lung squamous carcinoma, ovarian serous cystadenocarcinoma, skin cutaneous melanoma, castrate-resistant prostate cancer, Hodgkin lymphoma, serous and clear cell endometrial cancer, oral cancer, endometrial cancer, endocrine cancer, skin cancer, gastric cancer, esophageal cancer, laryngeal cancer, pancreatic cancer, colon cancer, bladder cancer, bone cancer, cervical cancer, uterine cancer, testicular cancer, rectal cancer, kidney cancer, liver cancer and lung cancer.

3. The use of claim 1 or 2, wherein the cancer is a lung cancer.

4. The use of any one of claims 1 to 3, wherein the cancer is a lung cancer selected from non-small cell lung cancer (NSCLC), adenocarcinoma, lung squamous cell carcinoma, large cell carcinoma, large cell neuroendocrine tumours, and small cell lung cancer (SCLC).

5. The use of any one of claims 1 to 4, wherein the cancer is a non-small cell lung cancer (NSCLC).

6. The use of any one of claims 1 to 5, wherein the EGFR inhibitor is afatinib or a pharmaceutically acceptable salt thereof.

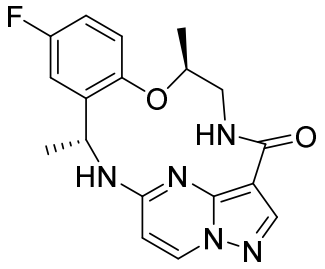
7. The use of any one of claims 1 to 5, wherein the EGFR inhibitor is dacomitinib or a pharmaceutically acceptable salt thereof.

8. The use of any one of claims 1 to 5, wherein the EGFR inhibitor is gefitinib, or a pharmaceutically acceptable salt thereof.

9. The use of any one of claims 1 to 5, wherein the EGFR inhibitor is osimertinib, or a pharmaceutically acceptable salt thereof.

10. The use of any one of claims 1 to 9, wherein the compound that inhibits FAK, SRC and JAK2, or pharmaceutically acceptable salt thereof, is to be present in 0.1 mg to 1 g daily dosage.

11. Use of a compound that inhibits FAK, SRC and JAK2, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament comprising a therapeutically effective amount of the compound, for treating cancer in a patient in combination with a therapeutically effective amount of an EGFR inhibitor selected from afatinib, dacomitinib, gefitinib and osimertinib, or a pharmaceutically acceptable salt thereof, wherein the compound that inhibits FAK, SRC and JAK2 is of the formula



or a pharmaceutically acceptable salt thereof.

12. The use of claim 11, wherein the cancer is selected from the group consisting of ALCL, NSCLC, neuroblastoma, inflammatory myofibroblastic tumor, adult renal cell carcinoma, pediatric renal cell carcinoma, breast cancer, ER^+ breast cancer, triple negative breast, colonic adenocarcinoma, glioblastoma, glioblastoma multiforme, anaplastic thyroid cancer, cholangiocarcinoma, ovarian cancer, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma, epithelioid hemangioendothelioma, intrahepatic cholangiocarcinoma, thyroid cancer, spitzoid neoplasms, sarcoma, astrocytoma, brain lower grade glioma, secretory breast carcinoma, mammary analogue carcinoma, acute myeloid leukemia, congenital mesoblastic nephroma, congenital fibrosarcomas, Ph-like acute lymphoblastic leukemia, thyroid

carcinoma, head and neck squamous cell carcinoma, pediatric glioma CML, prostate cancer, lung squamous carcinoma, ovarian serous cystadenocarcinoma, skin cutaneous melanoma, castrate-resistant prostate cancer, Hodgkin lymphoma, serous and clear cell endometrial cancer, oral cancer, endometrial cancer, endocrine cancer, skin cancer, gastric cancer, esophageal cancer, laryngeal cancer, pancreatic cancer, colon cancer, bladder cancer, bone cancer, cervical cancer, uterine cancer, testicular cancer, rectal cancer, kidney cancer, liver cancer and lung cancer.

13. The use of claim 11 or 12, wherein the cancer is a lung cancer.

14. The use of any one of claims 11 to 13, wherein the cancer is a lung cancer selected from non-small cell lung cancer (NSCLS), adenocarcinoma, lung squamous cell carcinoma, large cell carcinoma, large cell neuroendocrine tumors, and small cell lung cancer (SCLC).

15. The use of any one of claims 11 to 14, wherein the cancer is a non-small cell lung cancer (NSCLC).

16. The use of any one of claims 11 to 15, wherein the EGFR inhibitor is afatinib, or a pharmaceutically acceptable salt thereof.

17. The use of any one of claims 11 to 15, wherein the EGFR inhibitor is dacominitib, or a pharmaceutically acceptable salt thereof.

18. The use of any one of claims 11 to 15, wherein the EGFR inhibitor is gefitinib or a pharmaceutically acceptable salt thereof.

19. The use of any one of claims 11 to 15, wherein the EGFR inhibitor is osimertinib, or a pharmaceutically acceptable salt thereof.

20. The use of any one of claims 11 to 19, wherein the compound that inhibits FAK, SRC and JAK2, or pharmaceutically acceptable salt thereof, is to be present in the medicament in 0.1 mg to 1 g daily dosage.