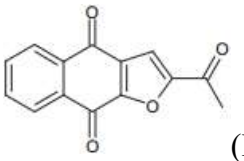
Claims

1. Use of a drug combination~~pharmaceutical combinatorial composition~~ in the manufacture of a medicament for the treatment of pancreatic cancer in a subject, the drug combination~~pharmaceutical combinatorial composition~~ comprising a therapeutically effective amount of the compound of formula (I):



(I),

or pharmaceutically acceptable salts and solvates thereof,

a low dose of gemcitabine or pharmaceutically acceptable salts and solvates thereof, and

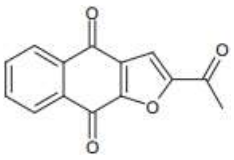
a weekly dose of therapeutically effective amount of paclitaxel or pharmaceutically acceptable salts and solvates thereof,

wherein,

the therapeutically effective amount of the compound of formula (I) or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of ~~about~~ 80 mg to ~~about~~ 960 mg per day, the low dose of gemcitabine or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of ~~about~~ 100 mg/m^2 to ~~about~~ 800 mg/m^2 by infusion per week, the therapeutically effective amount of paclitaxel or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of ~~about~~ 10 mg/m^2 to ~~about~~ 100 mg/m^2 by infusion per week,

wherein the pancreatic cancer is refractory to conventional chemotherapy and/or targeted therapies.

2. Use of a drug combination~~pharmaceutical combinatorial composition~~ in the manufacture of a medicament for resensitizing a subject with pancreatic cancer who has failed in at least one prior therap~~h~~y, the drug combination~~pharmaceutical combinatorial composition~~ comprising a therapeutically effective amount of the compound of formula (I):



(I),

or pharmaceutically acceptable salts and solvates thereof,

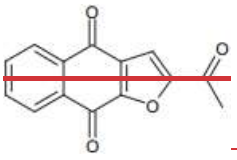
a low dose of gemcitabine or pharmaceutically acceptable salts and solvates thereof, and

a therapeutically effective amount of paclitaxel or pharmaceutically acceptable salts and solvates thereof,

wherein,

the therapeutically effective amount of the compound of formula (I) or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of ~~about~~ 80 mg to ~~about~~ 960 mg per day, the low dose of gemcitabine or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of ~~about~~ 100 mg/m^2 to ~~about~~ 800 mg/m^2 by infusion per week, the therapeutically effective amount of paclitaxel or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of ~~about~~ 10 mg/m^2 to ~~about~~ 100 mg/m^2 by infusion per week.

~~3. Use of a pharmaceutical combinatorial composition in the manufacture of a medicament for simultaneously inhibiting, reducing, and/or diminishing the survival and/or proliferation of cancer stem cells and heterogeneous cancer cells chosen from a subject with pancreatic cancer, the pharmaceutical composition combinatorial comprising a therapeutically effective amount of the compound of formula (I):~~



~~(I),~~

~~or pharmaceutically acceptable salts and solvates thereof,~~

~~a low dose of gemcitabine or pharmaceutically acceptable salts and solvates thereof, and~~

~~a therapeutically effective amount of paclitaxel or pharmaceutically acceptable salts and solvates thereof,~~

~~wherein,~~

~~the therapeutically effective amount of the compound of formula (I) or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of about 80 mg to about 960 mg per day, the low dose of gemcitabine or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of about 100 mg/m^2 to about 800 mg/m^2 by infusion per week, the therapeutically effective amount of paclitaxel or pharmaceutically acceptable salts and solvates thereof is to be administered at a dose of about 10 mg/m^2 to about 100 mg/m^2 by infusion per week.~~

34. The use according to ~~any one of~~ claims 1 ~~to~~ or 2~~3~~, wherein the pancreatic cancer is advanced, metastatic, unresectable, refractory or recurrent chemo-resistant cancer.

45. The use according to ~~any one of~~ claims 1 or~~to~~ 2~~3~~, wherein the subject is pancreatic cancer patient who has failed in at least one prior therapy.

56. The use according to ~~any one of~~ claims 1 or~~to~~ 2~~5~~, wherein the subject is metastatic pancreatic cancer patient who has progressed after at least one prior therapy.

67. The use according to claims 4~~5~~ or 5~~6~~, wherein the at least one prior therapy including at least one line systemic treatment, wherein the systemic treatment is selected from chemotherapy regimen.

78. The use according to claims 4~~5~~ or 5~~6~~, wherein the at least one prior therapy including first-line treatment, second-line treatment, or third-line treatment.

89. The use according to claims 4~~5~~ or 5~~6~~, wherein the at least one prior therapy is selected from the group consisting of gemcitabine-based monotherapy or combination chemotherapy, paclitaxel, FOLFIRINOX, mFOLFIRINOX and gemcitabine-Albumin paclitaxel regimens.

9~~10~~. The use according to any one of claims 1 to 8~~9~~, wherein the compound of

formula (I), the low dose of gemcitabine, and paclitaxel can be administered to the subject simultaneously, separately, and/or sequentially.

1011. The use according to any one of claims 1 to 89, wherein the compound of formula (I) is to be administered at a dose of ~~about~~ 80 mg to ~~about~~ 480 mg per day.

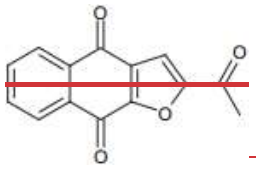
112. The use according to any one of claims 1 to 89, wherein the compound of formula (I) is to be administered in divided doses daily.

123. The use according to any one of claims 1 to 89, wherein the compound of formula (I) is to be administered at a dose of ~~about~~ 240 mg twice daily.

134. The use according to any one of claims 1 to 89, wherein the gemcitabine is to be administered as weekly infusion of ~~about~~ 600mg/m^2, ~~about~~ 550mg/m^2, ~~about~~ 500mg/m^2, ~~about~~ 450 mg/m^2, ~~about~~ 400mg/m^2, ~~about~~ 300mg/m^2, ~~about~~ 200mg/m^2,or ~~about~~ 100mg/m^2.

145. The use according to any one of claims 1 to 89, wherein the paclitaxel is to be administered as weekly infusion of ~~about~~ 80mg/m^2, ~~about~~ 70mg/m^2, ~~about~~ 60mg/m^2, ~~about~~ 50mg/m^2, ~~about~~ 40mg/m^2, ~~about~~ 30mg/m^2, ~~about~~ 20mg/m^2,or ~~about~~ 10mg/m^2.

~~16. A kit, comprising at least a compound of formula (I):~~



~~(I),~~

~~at least a gemcitabine, and~~

~~at least a paclitaxel.~~