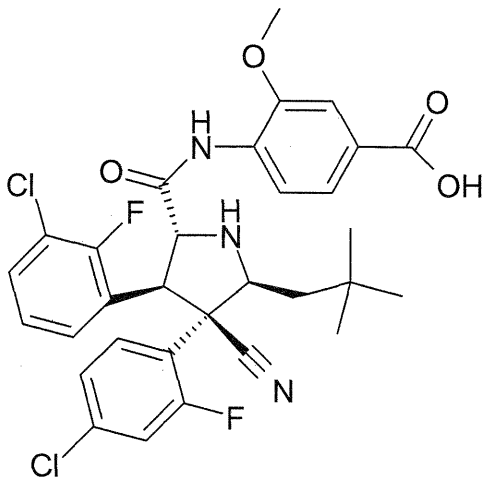
Inhibitors of the MDM2-p53 interaction have been shown to induce apoptosis in the established human AML cell line MOLM-13, which overexpresses MDM2 (K. Kojima, et. al., *Blood* **2005**, 106(9):3150-9). It has now been found that the combination of compounds of formula (I) together with Ara-C provide more than additive effects in disseminated MOLM-13 AML model in immunocompromised mice. Compounds of formula (I) and their preparation are disclosed in WO2013/135648. These compounds act as pro drugs of the compound



(A)

4-{[(2R,3S,4R,5S)-4-(4-Chloro-2-fluoro-phenyl)-3-(3-chloro-2-fluoro-phenyl)-4-cyano-5-(2,2-dimethyl-propyl)-pyrrolidine-2-carbonyl]-amino}-3-methoxy-benzoic acid (herein compound A).

Compound A is for example disclosed in US Patent No. 8,354,444 and WO2011/098398.

Summary ~~of the Invention~~

The present ~~invention~~ disclosure, in one aspect, relates to a pharmaceutical product comprising a) as a first component an inhibitor of the MDM2-p53 interaction (also "MDM2 inhibitor"); and b) as a second component cytarabine; as a combined preparation for the sequential or simultaneous use in the treatment of cancer.

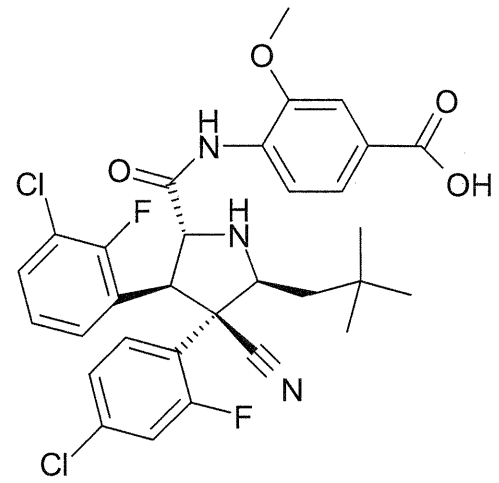
The present disclosure ~~invention~~ further relates to a method of treating a patient suffering from cancer, comprising administering to the patient the combination as mentioned above.

The present disclosure ~~invention~~ also relates to a kit comprising a) a first component which comprises, as an active agent, an inhibitor of the MDM2-p53 interaction; and b) a second component which comprises, as an active agent, the compound cytarabine.

In addition, the present disclosure ~~invention~~ relates to the use of an MDM2 inhibitor and cytarabine for the treatment of cancer.

A yet further aspect of the present disclosure ~~invention~~ is the use of an MDM2 inhibitor, and cytarabine ~~for~~ in the ~~preparation~~ manufacture of a medicament for the treatment of cancer.

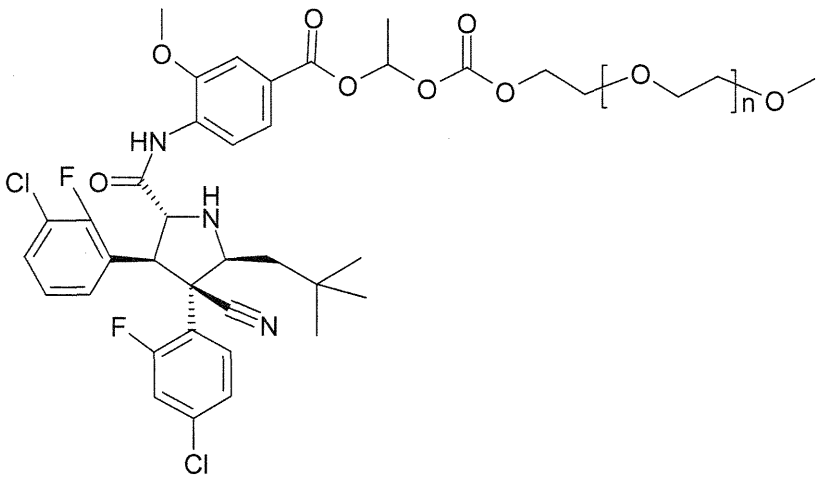
A yet further aspect of the present disclosure is a pharmaceutical product comprising, a) as a first component a compound of formula (I) as defined herein; and b) as a second component the compound cytarabine, wherein both components are administered intravenously, as a combined preparation for the simultaneous or sequential use in the treatment of cancer; characterized in that the dose of the compound of formula (I) corresponds to a dose of compound (A)



(A),

within the range from about 200 to about 1600 mg/day.

In one embodiment, the inhibitor of the MDM2-p53 interaction is selected from a compound of formula (I)



(I),

whereby the compounds of formula (I) are further specified herein.

Brief Description of the Drawings

Fig. 1 illustrates the antitumor efficacy of the compound I-B in combination with cytarabine on MOLM-13-luc.c4 (AML) tumor burden in SCID-beige mice, by quantification of bioluminescence.

7. The pharmaceutical product according to claim 1, wherein the inhibitor of the MDM2-p53 interaction is 4-{[(2R,3S,4R,5S)-3-(3-Chloro-2-fluoro-phenyl)-4-(4-chloro-2-fluoro-phenyl)-4-cyano-5-(2,2-dimethyl-propyl)-pyrrolidine-2-carbonyl]-amino}-3-methoxy-benzoic acid 1-mPEG-carbonyloxy-ethyl ester (mPEG, average MW, ~2200).

8. The pharmaceutical product according to any one of claims 1 to 7 for the treatment of Acute Myeloid Leukemia (AML).

9. The pharmaceutical product according to any one of claims 1 to 7 for the treatment of solid tumors.

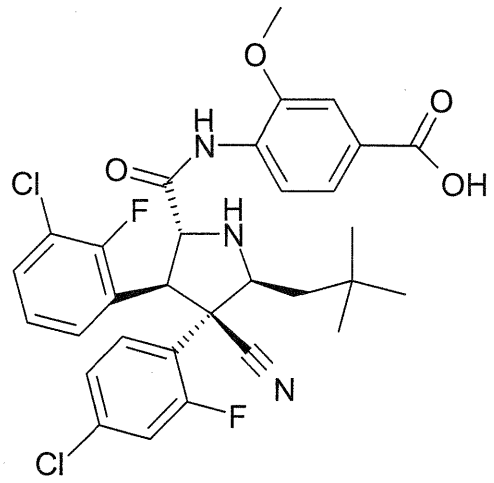
10. The use of a compound according to any one of claims 2 to 7 and cytarabine in the manufacture of a medicament ~~A method~~ for the treatment of cancer~~, comprising administering to a patient in need of such treatment an effective amount of a pharmaceutical product according to any one of claims 1 to 7~~.

11. The ~~method~~ use according to claim 10, wherein the cancer is Acute Myeloid Leukemia (AML).

12. The ~~method~~ use according to claim 10, wherein the cancer is a solid tumor.

~~13. The use of a compound according to any one of claims 2 to 7 and cytarabine for the manufacture of a medicament for the treatment of cancer, in particular Acute Myeloid Leukemia (AML).~~

~~14~~13. A pharmaceutical product comprising, a) as a first component a compound of formula (I) according to any one of claims 2 to 7; and b) as a second component the compound cytarabine, wherein both components are administered intravenously, as a combined preparation for the simultaneous or sequential use in the treatment of cancer; characterized in that the dose of the compound of formula (I) corresponds to a dose of compound (A)



(A),

within the range from about 200 to about 1600 mg/day.

~~15~~14. The pharmaceutical product according to claim ~~14~~13, wherein the compound of formula (I) is the compound 4-{[(2R,3S,4R,5S)-3-(3-Chloro-2-fluoro-phenyl)-4-(4-chloro-2-fluoro-phenyl)-4-cyano-5-(2,2-dimethyl-propyl)-pyrrolidine-2-carbonyl]-amino}-3-methoxy-benzoic acid 1-mPEG-carbonyloxy-ethyl ester (mPEG, average MW, ~2000).

~~16~~15. The pharmaceutical product according to claim ~~14~~13, wherein the compound of formula (I) is the compound 4-{[(2R,3S,4R,5S)-3-(3-Chloro-2-fluoro-phenyl)-4-(4-chloro-2-fluoro-phenyl)-4-cyano-5-(2,2-dimethyl-propyl)-pyrrolidine-2-carbonyl]-amino}-3-methoxy-benzoic acid 1-mPEG-carbonyloxy-ethyl ester (mPEG, average MW, ~2200).

~~17~~16. The pharmaceutical product according to any one of claims ~~14~~13 to ~~16~~15, wherein the compound of formula (I) is administered on days 1 to 5, followed by a 23 days rest perior of a 28 days treatment cycle.

~~18~~17. The pharmaceutical product according to claim ~~17~~16, wherein the compoud of formula (I) is administered once daily (qd) or two times a day (BID).

~~19~~18. The pharmaceutical product according to any one of claims ~~14~~13 to ~~18~~17, wherein the cancer is Acute Myeloid Leukemia (AML).