[0010] Citation or identification of any reference in Section 2 of this application is not to be construed as an admission that the reference is prior art to the present application.

3. SUMMARY

[0011] In one aspect, the present disclosure refers to use of a TOR kinase inhibitor in the manufacture of a medicament for treating E-twenty six (ETS) overexpressing Ewings sarcoma, comprising administration of an effective amount of a TOR kinase inhibitor to a patient having ETS overexpressing Ewings sarcoma. Provided herein are methods for treating or preventing E-twenty six (ETS) overexpressing Ewings sarcoma comprising administering an effective amount of a TOR kinase inhibitor to a patient having ETS overexpressing Ewings sarcoma.

[0012] In another aspect, the disclosure refers to a method for improving the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of a patient, comprising administration of an effective amount of a TOR kinase inhibitor to a patient having E-twenty six (ETS) overexpressing Ewings sarcoma. In certain ~~embodiments~~examples, provided herein are methods for improving the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of a patient, comprising administering an effective amount of a TOR kinase inhibitor to a patient having ETS overexpressing Ewings sarcoma.

[0013] In yet another aspect, the disclosure refers to use of a TOR kinase inhibitor in the manufacture of a medicament for inhibiting phosphorylation of S6RP, 4E-BP1 and/or AKT in a biological sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising administration of an effective amount of a TOR kinase inhibitor to said patient and comparing the amount of phosphorylated S6RP, 4E-BP1 and/or AKT in a biological sample of a patient obtained prior to and after administration of said TOR kinase inhibitor, wherein less phosphorylated S6RP, 4E-BP1 and/or AKT in said biological sample obtained after administration of said TOR kinase inhibitor relative to the amount of phosphorylated S6RP, 4E-BP1 and/or AKT in said biological sample obtained prior to administration of said TOR kinase inhibitor indicates inhibition. In some ~~embodiments~~examples, the TOR kinase inhibitor is a compound as described herein.

[0014] In a further aspect, the disclosure refers to use of a TOR kinase inhibitor in the manufacture of a medicament for inhibiting DNA-dependent protein kinase (DNA-PK) activity in a skin sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma,

comprising administration of an effective amount of a TOR kinase inhibitor to said patient and comparing the amount of phosphorylated DNA-PK in a biological sample of a patient obtained prior to and after administration of said TOR kinase inhibitor, wherein less phosphorylated DNA-PK in said biological sample obtained after administration of said TOR kinase inhibitor relative to the amount of phosphorylated DNA-PK in said biological sample obtained prior to administration of said TOR kinase inhibitor indicates inhibition.

In one aspect, the present disclosure refers to use of a TOR kinase inhibitor in the manufacture of a medicament for measuring inhibition of phosphorylation of S6RP, 4E-BP1 or AKT in a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising administration of an effective amount of a TOR kinase inhibitor to said patient, measuring the amount of phosphorylated S6RP, 4E-BP1 or AKT in said patient, and comparing said amount of phosphorylated S6RP, 4E-BP1 or AKT to that of said patient prior to administration of an effective amount of a TOR kinase inhibitor. In another aspect, the present disclosure refers to use of a TOR kinase inhibitor in the manufacture of a medicament for measuring inhibition of phosphorylation of DNA-PK S2056 in a skin sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising administration of an effective amount of a TOR kinase inhibitor to said patient, measuring the amount of phosphorylated DNA-PK S2056 present in the skin sample and comparing said amount of phosphorylated DNA-PK S2056 to that in a skin sample from said patient prior to administration of an effective amount of a TOR kinase inhibitor.

In yet another aspect, the present disclosure refers to a kit comprising a TOR kinase inhibitor and means for monitoring patient response to administration of said TOR kinase inhibitor, wherein said patient has E-twenty six (ETS) overexpressing Ewings sarcoma.

The present ~~embodiments~~examples can be understood more fully by reference to the detailed description and examples, which are intended to exemplify non-limiting ~~embodiments~~examples.

4. DETAILED DESCRIPTION

4.1 DEFINITIONS

[0015] An "alkyl" group is a saturated, partially saturated, or unsaturated straight chain or branched non-cyclic hydrocarbon having from 1 to 10 carbon atoms, typically from 1 to 8 carbons or, in some embodiments, from 1 to 6, 1 to 4, or 2 to 6 or carbon atoms. Representative

alkyl groups include -methyl, -ethyl, -n-propyl, -n-butyl, -n-pentyl and -n-hexyl; while saturated branched alkyls include -isopropyl, -*sec*-butyl, -isobutyl, -*tert*-butyl, -isopentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2,3-dimethylbutyl and the like. Examples of unsaturared alkyl groups include, but are not limited to, vinyl, allyl, -CH=CH(CH_3), -CH=C(CH_3)$_2$, -C(CH_3)=CH_2, -C(CH_3)=CH(CH_3), -C(CH_2CH_3)=CH_2, -C≡CH, -C≡C(CH_3), -C≡C(CH_2CH_3), -CH_2C≡CH, -CH_2C≡C(CH_3) and -CH_2C≡C(CH_7CH_3), among others. An alkyl group can be substituted or unsubstituted. In

CLAIMS

What is claimed is:

1. Use of a TOR kinase inhibitor in the manufacture of a medicament ~~A method~~ for treating E-twenty six (ETS) overexpressing Ewings sarcoma, comprising ~~administering~~administration of an effective amount of a TOR kinase inhibitor to a patient having ETS overexpressing Ewings sarcoma.

2. The ~~method~~ use of claim 1, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated.

3. The use ~~method~~ of claim 2, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated due to PTEN loss, a PIK3Ca mutation or EGFR overexpression, or a combination thereof.

4. The use ~~method~~ of claim 1, wherein said patient is to be administered about 0.5 mg/day to about 120 mg/day of a TOR kinase inhibitor.

5. The use ~~method~~ of claim 4, wherein said patient is to be administered 0.5 mg/day, 1 mg/day, 2 mg/day, 4 mg/day, 8 mg/day, 16 mg/day, 20 mg/day, 30 mg/day, 45 mg/day, 60 mg/day, 90 mg/day, or 120 mg/day of a TOR kinase inhibitor.

6. The use ~~method~~ of claim 1, wherein said patient is to be administered a unit dosage form comprising 0.25 mg, 1.0 mg 5.0 mg, 7.5 mg, or 10 mg of a TOR kinase inhibitor.

7. A method for improving the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of a patient, comprising ~~administering~~ administration of an effective amount of a TOR kinase inhibitor to a patient having E-twenty six (ETS) overexpressing Ewings sarcoma.

8. The method of claim 7, wherein the ETS overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated.

9. The method of claim 8, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated due to PTEN loss, a PIK3Ca mutation or EGFR overexpression, or a combination thereof.

10. Use of a TOR kinase inhibitor in the manufacture of a medicament~~A method~~ for inhibiting phosphorylation of S6RP, 4E-BP1 and/or AKT in a biological sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising ~~administering~~ administration of an effective amount of a TOR kinase inhibitor to said patient and comparing the amount of phosphorylated S6RP, 4E-BP1 and/or AKT in a biological sample of a patient obtained prior to and after administration of said TOR kinase inhibitor, wherein less phosphorylated S6RP, 4E-BP1 and/or AKT in said biological sample obtained after administration of said TOR kinase inhibitor relative to the amount of phosphorylated S6RP, 4E-BP1 and/or AKT in said biological sample obtained prior to administration of said TOR kinase inhibitor indicates inhibition.

11. The ~~method~~ use of claim 10, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated.

12. The use ~~method~~ of claim 11, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated due to PTEN loss, a PIK3Ca mutation or EGFR overexpression, or a combination thereof.

13. Use of a TOR kinase inhibitor in the manufacture of a medicament~~A method~~ for inhibiting DNA-dependent protein kinase (DNA-PK) activity in a skin sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising ~~administering~~ administration of an effective amount of a TOR kinase inhibitor to said patient and comparing the amount of phosphorylated DNA-PK in a biological sample of a patient obtained prior to and after administration of said TOR kinase inhibitor, wherein less phosphorylated DNA-PK in said biological sample obtained after administration of said TOR kinase inhibitor relative to the amount of phosphorylated DNA-PK in said biological sample obtained prior to administration of said TOR kinase inhibitor indicates inhibition.

14. The ~~method~~ use of claim 13, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated.

15. The use ~~method~~ of claim 14, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated due to PTEN loss, a PIK3Ca mutation or EGFR overexpression, or a combination thereof.

16. Use of a TOR kinase inhibitor in the manufacture of a medicament~~A method~~ for measuring inhibition of phosphorylation of S6RP, 4E-BP1 or AKT in a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising ~~administering~~ administration of an effective amount of a TOR kinase inhibitor to said patient, measuring the amount of phosphorylated S6RP, 4E-BP1 or AKT in said patient, and comparing said amount of phosphorylated S6RP, 4E-BP1 or AKT to that of said patient prior to administration of an effective amount of a TOR kinase inhibitor.

17. The ~~method~~ use of claim 16, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated.

18. The ~~method~~ use of claim 17, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated due to PTEN loss, a PIK3Ca mutation or EGFR overexpression, or a combination thereof.

19. Use of a TOR kinase inhibitor in the manufacture of a medicament~~A method~~ for measuring inhibition of phosphorylation of DNA-PK S2056 in a skin sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising ~~administering~~ administration of an effective amount of a TOR kinase inhibitor to said patient, measuring the amount of phosphorylated DNA-PK S2056 present in the skin sample and comparing said amount of phosphorylated DNA-PK S2056 to that in a skin sample from said patient prior to administration of an effective amount of a TOR kinase inhibitor.

20. The ~~method~~ use of claim 19, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated.

21. The ~~method~~ use of claim 20, wherein the E-twenty six (ETS) overexpressing Ewings sarcoma is that in which the PI3K/mTOR pathway is activated due to PTEN loss, a PIK3Ca mutation or EGFR overexpression, or a combination thereof.

22. ~~22.~~ A kit comprising a TOR kinase inhibitor and means for monitoring patient response to administration of said TOR kinase inhibitor, wherein said patient has E-twenty six (ETS) overexpressing Ewings sarcoma.