

CLAIMS

What is claimed is:

1. ~~A method for treating a solid tumor, non-Hodgkin lymphoma or multiple myeloma, comprising administering~~Use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) ~~to a patient having~~in the manufacture of a medicament for the treatment of a solid tumor, non-Hodgkin lymphoma or multiple myeloma.
2. The ~~method~~use of claim 1, wherein the solid tumor is an advanced solid tumor.
3. The ~~method~~use of claim 1, wherein the solid tumor is a neuroendocrine tumor.
4. The ~~method~~use of claim 3, wherein the neuroendocrine tumor is of gut origin, of non-pancreatic origin, or of unknown primary origin.
5. The ~~method~~use of claim 3, wherein the neuroendocrine tumor is a symptomatic endocrine producing tumor or a nonfunctional tumor.
6. The ~~method~~use of claim 3, wherein the neuroendocrine tumor is locally unresectable, metastatic moderate, well differentiated, low (grade 1) or intermediate (grade 2).
7. The ~~method~~use of claim 1, wherein the solid tumor is non-small cell lung cancer, glioblastoma multiforme, hepatocellular carcinoma, breast cancer, colorectal cancer, salivary cancer, pancreatic cancer, adenocystic cancer or adrenal cancer.
8. The ~~method~~use of claim 7, wherein the breast cancer is ER+/Her2-, ER+/Her2+, ER-/Her2+ or triple negative (TN).

9. ~~The method~~use of claim 1, wherein the non-Hodgkin lymphoma is diffuse large B-cell lymphoma.

10. ~~A method for achieving complete response, partial response or stable disease, as determined by the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) in a patient, comprising administering~~Use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) to a patient having a solid tumor~~in the manufacture of a medicament for achieving complete response, partial response or stable disease, as determined by the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) in a patient having a solid tumor.~~

11. ~~A method for achieving complete remission, partial remission or stable disease, as determined by the International Workshop Criteria (IWC) for non-Hodgkin lymphoma in a patient, comprising administering~~Use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) to patient having non-Hodgkin lymphoma~~in the manufacture of a medicament for achieving complete remission, partial remission or stable disease, as determined by the International Workshop Criteria (IWC) for non-Hodgkin lymphoma in a patient having non-Hodgkin lymphoma.~~

12. ~~A method for achieving a stringent complete response, complete response, or very good partial response, as determined by the International Uniform Response Criteria for Multiple Myeloma (IURC) in a patient, comprising administering~~Use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) to patient having multiple myeloma~~in the manufacture of a medicament for achieving a stringent complete response, complete response, or very good partial response, as determined by the International Uniform Response Criteria for Multiple Myeloma (IURC) in a patient having multiple myeloma.~~

13. ~~A method for improving, Eastern Cooperative Oncology Group Performance Status (ECOG) or Response Assessment for Neuro-Oncology (RANO) Working Group for glioblastoma multiforme in a patient, comprising administering~~Use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) to a patient having non-Hodgkin lymphoma, multiple myeloma or glioblastoma multiforme~~in the manufacture of a medicament for improving, Eastern Cooperative Oncology Group Performance Status (ECOG) or Response Assessment for Neuro-Oncology (RANO) Working Group for glioblastoma multiforme in a patient having non-Hodgkin lymphoma, multiple myeloma or glioblastoma multiforme.~~

14. The ~~method~~use of any one of claims 1 – 13, wherein the TOR kinase inhibitor is a compound from Table A, B, C or D.

15. A TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) for use in therapy.

16. The TOR kinase inhibitor of claim 15, wherein the TOR kinase inhibitor is a compound from Table A, B, C or D.

[0011] In certain embodiments, provided herein are methods for achieving a Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of complete response, partial response or stable disease, improving International Workshop Criteria (IWC) for NHL, improving International Uniform Response Criteria for Multiple Myeloma (IURC), improving Eastern Cooperative Oncology Group Performance Status (ECOG) or improving Response Assessment for Neuro-Oncology (RANO) Working Group for GBM comprising administering an effective amount of a TOR kinase inhibitor to a patient having a solid tumor, non-Hodgkin lymphoma or multiple myeloma. In some embodiments, the TOR kinase inhibitor is a compound as described herein.

[0011a] In a first aspect, there is provided a use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) in the manufacture of a medicament for the treatment of a solid tumor, non-Hodgkin lymphoma or multiple myeloma.

[0011b] In a second aspect, there is provided a use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) in the manufacture of a medicament for achieving complete response, partial response or stable disease, as determined by the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) in a patient having a solid tumor.

[0011c] In a third aspect, there is provided a use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) the manufacture of a medicament for achieving complete remission, partial remission or stable disease, as determined by the International Workshop Criteria (IWC) for non-Hodgkin lymphoma in a patient having non-Hodgkin lymphoma.

[0011d] In a fourth aspect, there is provided a use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) in the manufacture of a medicament for achieving a stringent complete response, complete response, or very good partial response, as determined by the International Uniform Response Criteria for Multiple Myeloma (IURC) in a patient having multiple myeloma.

[0011e] In a fifth aspect, there is provided a use of an effective amount of a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) in the manufacture of a medicament for improving Eastern Cooperative Oncology

Group Performance Status (ECOG) or Response Assessment for Neuro-Oncology (RANO) Working Group for glioblastoma multiforme in a patient having non-Hodgkin lymphoma, multiple myeloma or glioblastoma multiforme.

[0011f] In a sixth aspect, there is provided a TOR kinase inhibitor of formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig), (II), (IIa), (IIb), (IIc), (IId), (III), or (IV) for use in therapy.

[0012] The present embodiments can be understood more fully by reference to the detailed description and examples, which are intended to exemplify non-limiting embodiments.

1. DETAILED DESCRIPTION

1.1 DEFINITIONS

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 unsaturated alkyl groups include, but are not limited to, vinyl, allyl, -CH=CH(CH₃), -CH=C(CH₃)₂, -C(CH₃)=CH₂, -C(CH₃)=CH(CH₃), -C(CH₂CH₃)=CH₂, -C≡CH, -C≡C(CH₃), -C≡C(CH₂CH₃), -CH₂C≡CH, -CH₂C≡C(CH₃) and -CH₂C≡C(CH₂CH₃), among others. An alkyl group can be substituted or unsubstituted. In certain embodiments, when the alkyl groups described herein are said to be “substituted,” they may be substituted with any substituent or substituents as those found in the exemplary compounds and embodiments disclosed herein, as well as halogen (chloro, iodo, bromo, or