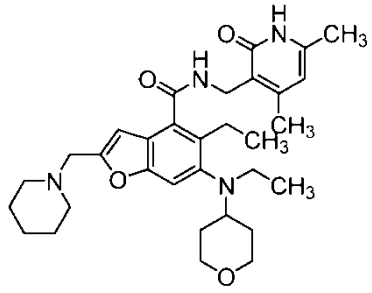
conclusion, the efficacy of traditional chemotherapy in relapsed or refractory PTCL is not ideal. Histone deacetylase (HDAC) inhibitors and folic acid inhibitors are approved for use in such patients, but the improvement of efficacy is limited. At present, more new and effective drugs need to be developed and marketed to improve the prognosis of patients with relapsed or refractory PTCL.

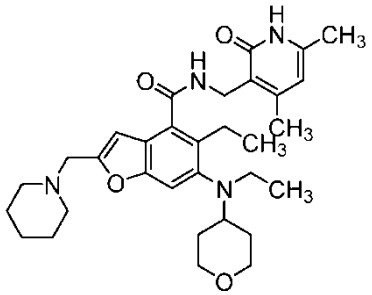
Summary

In a first aspect of the present disclosure, there is provided a use of a compound shown in Formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of T-cell lymphoma:



(I)

The present disclosure provides the use of a compound shown in Formula (I) or a pharmaceutically acceptable salt thereof in the preparation of drugs for the treatment of T-cell lymphoma:



(I)

In some examples, the T-cell lymphoma of the present disclosure is peripheral T-cell lymphoma (mature T- and NK-cell lymphoma).

In some examples, the T-cell lymphoma of the present disclosure is angioimmunoblastic T-cell lymphoma (AITL), anaplastic large cell lymphoma (ALCL), peripheral T lymphoma-non-specific (PTCL-NOS), or NK/T-cell lymphoma (NKTCL).

In some examples, the T-cell lymphoma of the present disclosure is an angioimmunoblastic T-cell lymphoma or a peripheral T-lymphoma, not otherwise specified.

In some examples, the T-cell lymphoma of the present disclosure is angioimmunoblastic T-cell lymphoma.

In some examples, the T-cell lymphoma of the present disclosure is a peripheral T lymphoma, not otherwise specified.

In some examples, the T-cell lymphoma of the present disclosure is relapsed/refractory peripheral T-cell lymphoma.

In some examples, the T-cell lymphoma of the present disclosure is peripheral T-cell lymphoma which has undergone first-line chemotherapy.

In some examples, the T-cell lymphoma of the present disclosure is a peripheral T-cell lymphoma which has undergone at least one treatment selected from histone deacetylase inhibitors, folic acid metabolism inhibitors, or anti-CD30 monoclonal antibodies.

In some examples, the T-cell lymphoma of the present disclosure is a peripheral T-cell lymphoma which has undergone first-line chemotherapy and at least one treatment selected from histone deacetylase inhibitors, folic acid metabolism inhibitors, or anti-CD30 monoclonal antibodies.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 1–800mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from

2.5mg, 5.0mg, 7.5mg, 10.0mg, 12.5mg, 15.0mg, 17.5mg, 20.0mg, 22.5mg, 25.0mg, 27.5 mg, 30.0mg, 32.5mg, 35.0mg, 37.5mg, 40.0mg, 42.5mg, 45.0mg, 47.5mg, 50.0mg, 52.5 mg, 55.0mg, 57.5mg, 60.0mg, 62.5mg, 65.0mg, 67.5mg, 70.0mg, 72.5mg, 75.0mg, 77.5 mg, 80.0mg, 82.5mg, 85.0mg, 87.5mg, 90.0mg, 92.5mg, 95.0mg, 97.5mg, 100.0mg, 102 .5mg, 105.0mg, 107.5mg, 110.0mg, 112.5mg, 115.0mg, 117.5mg, 120.0mg, 122.5mg, 1 25.0mg, 127.5mg, 130.0mg, 132.5mg, 135.0mg, 137.5mg, 140.0mg, 142.5mg, 145.0mg , 147.5mg, 150.0mg, 152.5mg, 155.0mg, 157.5mg, 160.0mg, 162.5mg, 165.0mg, 167.5 mg, 170.0mg, 172.5mg, 175.0mg, 177.5mg, 180.0mg, 182.5mg, 185.0mg, 187.5mg, 190 .0mg, 192.5mg, 195.0mg, 197.5mg, 200.0mg, 202.5mg, 205.0mg, 207.5mg, 210.0mg, 2 12.5mg, 215.0mg, 217.5mg, 220.0mg, 222.5mg, 225.0mg, 227.5mg, 230.0mg, 232.5mg , 235.0mg, 237.5mg, 240.0mg, 242.5mg, 245.0mg, 247.5mg, 250.0mg, 252.5mg, 255.0 mg, 257.5mg, 260.0mg, 262.5mg, 265.0mg, 267.5mg,

697.5mg, 700.0mg, 702.5mg, 705.0mg, 707.5mg, 710.0mg, 712.5mg, 715.0mg, 717.5mg, 720.0mg, 722.5mg, 725.0mg, 727.5mg, 730.0mg, 732.5mg, 735.0mg, 737.5mg, 740.0mg, 742.5mg, 745.0mg, 747.5mg, 750.0mg, 752.5mg, 755.0mg, 757.5mg, 760.0mg, 762.5mg, 765.0mg, 767.5mg, 770.0mg, 772.5mg, 775.0mg, 777.5mg, 780.0mg, 782.5mg, 785.0mg, 787.5mg, 790.0mg, 792.5mg, 795.0mg, 797.5mg or 800.0mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 50mg, 75mg, 100mg, 125mg, 150mg, 175mg, 200mg, 225mg, 250mg, 275mg, 300mg, 350mg, 375mg, 400mg, 425mg, 450mg, 475mg, 500mg, 525mg, 550mg, 575mg, or 600mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 50mg, 100mg, 200mg, 300mg, 350mg, or 400mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 200mg, 300mg, or 350mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is 200mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is 300mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is 350mg, administered once or twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 200mg, 300mg, or 350mg, administered twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is 200mg, administered twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is 300mg, administered twice a day.

In some examples, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is 350mg, administered twice a day.

Another example of the present disclosure provides a method of treating T-cell lymphoma, in which patients are given a therapeutically effective amount of a compound shown in Formula (I) or a pharmaceutically acceptable salt thereof.

Another example of the present disclosure provides a method of treating T-cell lymphoma, in which 1mg to 800mg of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is administered to patients once or twice a day.

In some examples, the present disclosure provides a method of treating T-cell lymphoma, in which there is a 28-day dosing cycle.

Another example of the present disclosure provides a compound shown in Formula (I) for use in treating T-cell lymphoma, or a pharmaceutically acceptable salt thereof.

The term “patient” as used in the present disclosure means a human.

The acetylase inhibitors described in the present disclosure include but are not limited to chidamide, belimistat, or romidesin. The folic acid metabolism inhibitors include but are not limited to prasa. The anti-CD30 antibodies include but are not limited to brentuximab vedotin.

Another example of the present disclosure provides a pharmaceutical composition comprising a compound shown in Formula (I) or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers. The pharmaceutical composition may be specially formulated in solid or liquid form for oral administration or for local administration.

The present disclosure further provides the use of a composition comprising a compound shown in Formula (I) or a pharmaceutically acceptable salt thereof with one or more pharmaceutically acceptable carriers in the preparation of a medicament for the treatment of T-cell lymphoma.

“Pharmaceutically acceptable carrier” as described in this disclosure means any type of non-toxic inert solid, semi-solid or liquid filler, diluent, encapsulating material, or formulation excipient. Some examples of substances that may be pharmaceutically acceptable carriers are sugars, such as: Lactose or cellulose and derivatives thereof, such as sodium carboxymethyl cellulose, ethyl cellulose, and cellulose acetate.

In an optional example, patients in the present disclosure have been treated with first-line chemotherapy and at least one new drug (chidamide, prasa, brentuximab vedotin), wherein:

–CD30 systemic ALCL: Treated with brentuximab vedotin

–NKTCL: Treated with asparaginase/peraspartase regimen

–Other subtypes: Treated with CHOP or CHOP-like regimen (including but not limited to CHOEP, BV+CHP).

When relapsed/refractory is mentioned in the present disclosure, relapse refers to occurrence of progressive disease after the last-line treatment response, and refractory refers to failure of response of the last treatment.

ORR: Defined as the proportion of subjects with best efficacy of CR or PR from the start of the first dose to the occurrence of PD or the start of subsequent new anti-tumor treatment, whichever occurs first.

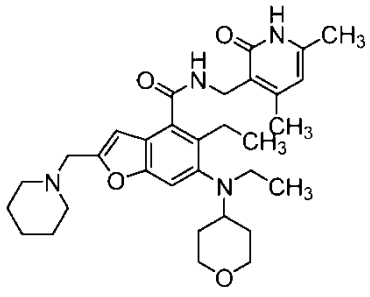
PFS: Defined as the date from the first dose to the first documented PD or death due to any cause, whichever occurs first. If the subject still does not experience PD or death as of the data cutoff date, the cutoff date is the date of the subject’s last efficacy assessment. If the subject does not undergo tumor evaluation, the cut-off date is the date of first drug administration, and the PFS lasts for 1 day.

DoR: Defined as the time from the first assessment of CR or PR to the first assessment of PD or death due to any cause, whichever occurs first. If the subject still did not experience PD or death as of the data cut-off date, the cut-off date is the date of the subject’s last efficacy assessment. Only for subjects who achieved CR or PR.

Progressive disease is defined as worsening of a subject’s condition due to the indication under study. Including radiographic progression, progression of test results, and progression of clinical symptoms and signs. The appearance of new lesions or progression of existing lesions is considered to be progressive disease. Events that are life-threatening, require hospitalization or

Claims

1. Use of a compound shown in Formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of T-cell lymphoma:



(I)

2. The use according to Claim 1, wherein the T-cell lymphoma is peripheral T-cell lymphoma (mature T and NK cell lymphoma), preferably angioimmunoblastic T-cell lymphoma, anaplastic large cell lymphoma, peripheral T lymphoma-non-specific or NK/T-cell lymphoma, most preferably angioimmunoblastic T-cell lymphoma or peripheral T lymphoma-non-specific.

3. The use according to Claim 2, wherein the peripheral T-cell lymphoma is relapsed/refractory peripheral T-cell lymphoma.

4. The use according to Claim 2, wherein the peripheral T-cell lymphoma is a peripheral T-cell lymphoma which has undergone first-line chemotherapy and/or at least one treatment selected from histone deacetylase inhibitors, folic acid metabolism inhibitors, or anti-CD30 monoclonal antibodies, preferably, the peripheral T-cell lymphoma is a peripheral T-cell lymphoma which has undergone first-line chemotherapy, or first-line chemotherapy and at least one treatment selected from histone deacetylase inhibitors, folic acid metabolism inhibitors, or anti-CD30 monoclonal antibodies.

5. The use according to any one of Claims 1-4, wherein the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is

selected from 1mg to 800mg, to be administered once or twice a day.

6. The use according to Claim 5, wherein the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 50mg, 75mg, 100mg, 125mg, 150mg, 175mg, 200mg, 225mg, 250mg, 275mg, 300mg, 350mg, 375mg, 400mg, 425mg, 450mg, 475mg, 500mg, 525mg, 550mg, 575mg, or 600mg, to be administered once or twice a day, preferably, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 50mg, 100mg, 200mg, 300mg, 350mg, or 400mg, to be administered once or twice a day, or most preferably, the administered dose of the compound shown in Formula (I) or a pharmaceutically acceptable salt thereof is selected from 200mg, 300mg, or 350mg, to be administered once or twice a day.