METHODS AND COMPOSITIONS FOR TREATING ADVANCED STAGE NON-SMALL CELL LUNG CANCER

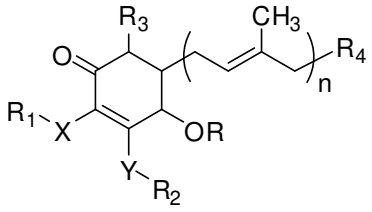
BACKGROUND OF THE INVENTION

[0001] Lung cancer is the most frequently diagnosed major cancer in the world and leading cause of cancer mortality worldwide. In the United States of America (USA), it was estimated that 219,440 new cases of lung cancer (116,090 men and 103,350 women) were diagnosed and 159,390 deaths were related to this malignancy in 2009. In Taiwan, 8,748 new cases of lung cancer were diagnosed in 2006, accounting for 11.94% of cancer diagnoses, and 7,479 patients died of this disease, contributing to 19.68% cancer deaths. The mortality was 44.42 and 20.65 per 100,000 men and women, respectively.

[0002] Lung cancers are categorized on the basis of important prognostic and therapeutic implications as either non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC). Non-small cell lung cancer contributed to about 80% of new cases diagnosed each year. NSCLC typically proliferates slower with lower doubling time than SCLC and can be characterized as three primary histologic types: adenocarcinoma, squamous cell, and large cell carcinoma. Adenocarcinoma has become the dominant histologic type of NSCLC and is the most common type in women and non-smokers. It typically arises in the periphery with glandular differentiation or mucin production, forms tubular or papillary structures, and metastasizes widely and early, compared to squamous carcinoma.

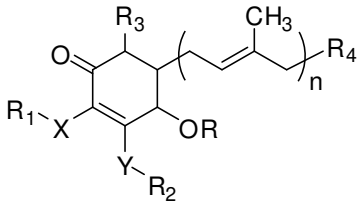
[0003] About 70% of NSCLC patients are diagnosed with advanced, poor-prognosis stage III or IV disease (approximately 50% for stage IV). The majority of these advanced tumors are considered inoperable due to disseminated (multiple sites) metastatic disease or metastatic sites that are not amendable to local therapy.

SUMMARY

[0003a] In one aspect, present disclosure refers to the use of a therapeutically effective amount of a cyclohexenone compound having the structure:  in the manufacture of a medicament for (1) selecting for treatment of a patient with advanced stage lung cancer wherein said patient is KRAS positive and (2) treating a subject with advanced stage lung cancer, wherein each of X and Y is oxygen; R is a hydrogen or $C(=O)C_1$-C_8alkyl; each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3; R_4 is hydrogen; m=1-12, n=1-12; or a pharmaceutically acceptable salt, or solvate thereof. In another example, there is disclosed the use of a therapeutically

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of a cyclohexenone compound having the structure:  in the manufacture of a medicament for (1) selecting for treatment of a patient with advanced stage lung cancer wherein said patient is KRAS positive and (2) treating a subject with advanced stage lung cancer,

wherein each of X and Y is oxygen;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is hydrogen; m=1-12,

n=1-12; or a pharmaceutically acceptable salt, or solvate thereof.

2. The use of claim 1, wherein said advanced stage lung cancer is non-small cell lung cancer stage IV.

3. The use of claim 2, wherein the medicament improves or maintains the quality of life of said patient diagnosed with non-small cell lung cancer stage IV

4. The use of claims 1-4, wherein the medicament is in a dosage regimen of 50-450 mg per day.

5. The use of claims 1-4, wherein said individual is a patient who has failed at least two lines of anti-cancer therapy.

6. The use of any one of claims 1-5, wherein said cyclohexenone compound, or a pharmaceutically acceptable salt, or solvate thereof, is to be used parenterally, intravenously, orally, or by injection.

7. The use of claim 6, wherein the medicament is in a dosage regiment of about 100-300 mg per day.

8. The use of any one of claims 1-7, wherein said individual is cancer free after 12 weeks of administration of said compound.

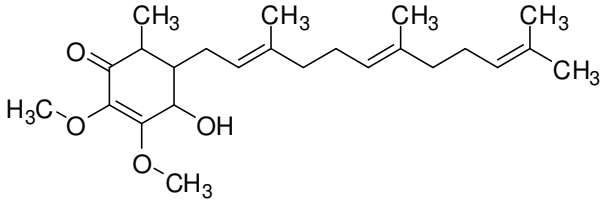
9. The use of any one of claims 1-8, wherein said compound is isolated from *Antrodia camphorata.*

10. The use of any one of claims 1-9, wherein R is a hydrogen or $C(=O)CH_3$.

11. The use of any one of claims 1-10, wherein R_1 is a hydrogen or methyl.

12. The use of any one of claims 1-11, wherein R_2 is a hydrogen or methyl.

13. The use of any one of claims 1-12, wherein said compound is



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