Methods for treating lung disorders

Cross Reference

This application claims priority to U.S. Provisional Patent Application Serial Nos. 62/519257 filed June 14, 2017; 62/628582 filed February 9, 2018; 62/653942 filed April 6, 2018; and 62/678387 filed May 31, 2018, each incorporated by reference herein in their entirety.

Background

Lung cancer is the second most common cancer and one of the most lethal. Conventional therapies such as surgical resection, radiation, and chemotherapy have not resulted in satisfactory long-term survival rates. Systemic drug delivery, even at a high dose, results in only a limited amount of taxane drugs reaching lung tumors. Improved methods for treating lung tumors are thus needed.

Summary

In one aspect, the present disclosure refers to the use of a composition in the manufacture of a medicament for treating a lung tumor, wherein the composition comprises taxane particles and a pharmaceutically acceptable carrier in a suspension, wherein the composition is to be pulmonary administered to the subject by aerosolization and nebulization, wherein the taxane particles in the composition comprise at least 95% of the taxane and have a mean particle size (number) of between 0.1 µm and 5 µm, wherein the taxane particles have a specific surface area (SSA) of at least 12 m^2/g.

In one example, the disclosure provides methods for treating a lung disorder, such as a lung tumor or pulmonary fibrosis, comprising pulmonary administration to a subject with a lung disorder of an amount effective of a composition comprising taxane particles to treat the lung disorder, wherein the taxane particles comprise at least 95% of the taxane and have a mean particle size (number) of between 0.1 µm and 5 µm. In one example, the pulmonary administration may comprise nebulization, wherein the nebulizing results in pulmonary

We claim

1. Use of a composition in the manufacture of a medicament for treating a lung tumor, wherein the composition comprises taxane particles and a pharmaceutically acceptable carrier in a suspension, wherein the composition is to be pulmonary administered to the subject by aerosolization and nebulization, wherein the taxane particles in the composition comprise at least 95% of the taxane and have a mean particle size (number) of between 0.1 µm and 5 µm, wherein the taxane particles have a specific surface area (SSA) of at least 12 m^2/g.

2. The use of claim 1, wherein the taxane particles have a mean particle size (number) of between 0.4 µm and 3 µm.

3. The use of any one of claims 1-2, wherein the taxane particles have a mean particle size (number) of between 0.4 µm and 1.2 µm.

4. The use of any one of claims 1-3, wherein the taxane particles have a specific surface area (SSA) of at least 18 m^2/g.

5. The use of any one of claims 1-4, wherein the suspension further comprises a polysorbate, wherein the polysorbate is present in the suspension at a concentration of between 0.01% v/v and 1.5% v/v.

6. The use of claim 5, wherein the pharmaceutically acceptable carrier is saline.

7. The use of claim 5 or 6, wherein the polysorbate is polysorbate 80.

8. The use of any one of claims 5-7, wherein the taxane is present in the suspension at a concentration between 1 mg/ml and 40 mg/ml.

9. The use of any one of claims 1-8, wherein the taxane particles are uncoated and exclude lipids, polymers, proteins, polyethoxylated castor oil, and polyethylene glycol

glycerides composed of mono-, di- and triglycerides and mono- and diesters of polyethylene glycol.

10. The use of any one of claims 1-9, wherein the taxane comprises paclitaxel, docetaxel, cabazitaxel, or a pharmaceutically acceptable salt thereof.

11. The use of claim 10, wherein the taxane comprises paclitaxel or a pharmaceutically acceptable salt thereof.

12. The use of claim 1, wherein the taxane particles have a mean bulk density between 0.050 g/cm^3 and 0.12 g/cm^3.

13. The use of claim 10, wherein the taxane comprises docetaxel or a pharmaceutically acceptable salt thereof.

14. The use of any one of claims 1-13, wherein the taxane remains detectable in lung tissue of the subject for at least 4 days after administration.

15. The use of any one of claims 1-14, wherein the taxane particles are in crystalline form.

16. The use of any one of claims 1-15, wherein the aerosol droplets have a mass median aerodynamic diameter (MMAD) of between 0.5 µm to 6 µm diameter.

17. The use of any one of claims 1-16, wherein the taxane particles reside at the tumor site after administration of the composition exposing the tumor to the taxane particles for a sustained amount of time sufficient to stimulate the endogenous immune system of the subject resulting in the production of tumoricidal cells and infiltration of the tumoricidal cells into the tumor at a level sufficient to treat the tumor.

18. The use of claim 17, wherein the sustained amount of time is at least 4 weeks.

19. The use of any one of claims 17-18, wherein the tumoricidal cells comprise T-cells, B cells, or natural killer (NK) cells, or combinations thereof.

20. The use of any one of claims 1-19, wherein the composition is to be administered in two or more separate administrations.

21. The use of claim 20, wherein the composition is to be administered once a week for at least two weeks.

22. The use of claim 20, wherein the composition is to be administered twice a week for at least one week, wherein the two or more separate administrations are separated by at least one day.

23. The use of any one of claims 1-22, wherein the treatment of the tumor is elimination of the tumor.