pancreatic neuroendocrine tumors, advanced renal cell carcinoma, and subependymal giant cell astrocytoma (SEGA) associated with Tuberous Sclerosis. The mode of action of sirolimus is to bind the cytosolic protein FK-binding protein 12 (FKBP12), and the sirolimus-FKBP12 complex in turn inhibits the mTOR pathway by directly binding to the mTOR Complex 1 (mTORC1).

[0005] Albumin-based nanoparticle compositions have been developed as a drug delivery system for delivering substantially water insoluble drugs. *See*, for example, U. S. Pat. Nos.5,916,596; 6,506,405; 6,749,868, and 6,537,579, 7,820,788, and 7,923,536. Abraxane®, an albumin stabilized nanoparticle formulation of paclitaxel, was approved in the United States in 2005 and subsequently in various other countries for treating metastatic breast cancer. It was recently approved for treating non-small cell lung cancer in the United States, and has also shown therapeutic efficacy in various clinical trials for treating difficult-to-treat cancers such as bladder cancer and melanoma. Albumin derived from human blood has been used for the manufacture of Abraxane® as well as various other albumin-based nanoparticle compositions.

[0006] The disclosures of all publications, patents, patent applications and published patent applications referred to herein are hereby incorporated herein by reference in their entirety.

SUMMARY

[0006a] In a first aspect, there is provided use of an effective amount of a composition comprising nanoparticles comprising an mTOR inhibitor and an albumin in the manufacture of a medicament for treating a hematological malignancy in an individual, wherein said medicament is to be administered to an individual in combination with an effective amount of an immunomodulator.

[0007] The present disclosure provides methods of treating a hematological malignancy (such as lymphoma, leukemia, and myeloma) in an individual, comprising administering to the individual a) an effective amount of a composition comprising nanoparticles comprising an mTOR inhibitor (such as a limus drug, *e.g.*, sirolimus or a derivative thereof) and an albumin; and b) an effective amount of a second therapeutic agent. In some embodiments, the mTOR inhibitor nanoparticle composition (such as sirolimus/albumin nanoparticle composition) and the second therapeutic agent act synergistically to inhibit cell proliferation. In some embodiments, the mTOR inhibitor is a limus drug. In some embodiments, the mTOR inhibitor is sirolimus or a derivative thereof. In some embodiments, the mTOR inhibitor is sirolimus. In some embodiments, the albumin is human albumin (such as human serum albumin). In some embodiments, the nanoparticles comprise sirolimus or a derivative thereof associated (*e.g.*, coated) with albumin. In some embodiments, the nanoparticles comprise sirolimus or a derivative thereof coated with albumin. In some embodiments, the average particle size of the nanoparticles in the mTOR inhibitor nanoparticle composition (such as sirolimus/albumin nanoparticle composition) is no greater than about 150 nm (such as no greater than about 120

CLAIMS

What is claimed is:

1. Use of an effective amount of a composition comprising nanoparticles comprising an mTOR inhibitor and an albumin in the manufacture of a medicament for treating a hematological malignancy in an individual, wherein said medicament is to be administered to an individual in combination with an effective amount of an immunomodulator.
2. The use of claim 1, wherein the hematological malignancy is multiple myeloma, mantle cell lymphoma, T cell lymphoma, chronic myeloid leukemia, or acute myeloid leukemia.
3. The use of claim 1 or claim 2, wherein the hematological malignancy is relapsed or refractory to a standard therapy for the hematological malignancy.
4. The use of any one of claims 1-3, wherein the amount of the mTOR inhibitor in the mTOR inhibitor nanoparticle composition is from 10 mg/m^2 to 150 mg/m^2.
5. The use of any one of claims 1-4, wherein the mTOR inhibitor nanoparticle composition is to be administered weekly or 3 out of every 4 weeks.
6. The use of any one of claims 1-5, wherein the mTOR inhibitor nanoparticle composition and the immunomodulator are to be administered sequentially or simultaneously to the individual.
7. The use of any one of claims 1-6, wherein the mTOR inhibitor is a limus drug.
8. The use of claim 7, wherein the limus drug is sirolimus.
9. The use of any one of claims 1-8, wherein the average diameter of the nanoparticles in the composition is no greater than 150 nm.
10. The use of any one of claims 1-9, wherein the weight ratio of the albumin to the mTOR inhibitor in the nanoparticle composition is no greater than 9:1.
11. The use of any one of claims 1-10, wherein the nanoparticles comprise the mTOR inhibitor coated with the albumin.
12. The use of any one of claims 1-11, wherein the mTOR inhibitor nanoparticle composition is to be administered intravenously.
13. The use of any one of claims 1-12, wherein the individual is human.

14. The use of any one of claims 1-13, wherein the individual is selected for treatment based on the presence of at least one mTOR-activating aberration.
15. The use of any one of claims 1-14, wherein the immunomodulator is an IMiDs®.
16. The use of any one of claims 1-14, wherein the immunomodulator is an immune checkpoint inhibitor.
17. The use of any one of claims 1-14, wherein the immunomodulator is pomalidomide.
18. The use of any one of claims 1-14, wherein the immunomodulator is lenalidomide.