a study of 15 patients, the combination of docetaxel with mitomycin and irinotecan produced no response and the median overall survival was 24 weeks. Clinical benefits were not reported in any of these studies. Almhanna et al., *Oncology*, 22:10 (2008).

[0008] Albumin bound paclitaxel (e.g., ABRAXANE®) in combination with gemcitabine was found to be well tolerated in advanced pancreatic cancer in a Phase I/II study and showed evidence of antitumor activity. See, for example, US Patent App.; No. 2006/0263434; Maitra et al., *Mol. Cancer Ther.* 8(12 Suppl):C246 (2009); Loehr et al., *J. of Clinical Oncology* 27(15S)(May 20 Supplement):200, Abstract No. 4526 (2009); Von Hoff et al., *J. of Clinical Oncology* 27(15S)(May 20 Supplement), Abstract No. 4525 (2009); and Kim et al., *Proc. Amer. Assoc. Cancer Res*., 46, Abstract No. 1440 (2005). .

[0009] The disclosures of all publications, patents, patent applications and published patent applications referred to herein are hereby incorporated herein by reference in their entirety.

BRIEF SUMMARY

[0010] The present disclosure in some embodiments provides a method of treating pancreatic cancer (such as advanced pancreatic cancer) in an individual in need thereof, comprising (or consisting of or consisting essentially of) administering to the individual an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin (hereinafter also referred to as "the nanoparticle composition" or "taxane nanoparticle composition"), wherein the individual has been previously treated for pancreatic cancer (hereinafter also referred to "the prior therapy").

[0010a] In one aspect, there is provided use of a composition comprising nanoparticles comprising a taxane and an albumin in the manufacture of a medicament for treating pancreatic cancer in an individual in need thereof, wherein the individual has progressed on a gemcitabine-based therapy, wherein a prior therapy has stopped for at least 6 months when initiating administration of the medicament to the individual, and wherein the treatment is in combination with gemcitabine.

[0011] In some embodiments, the prior therapy comprises administration of gemcitabine ("a gemcitabine-based therapy"). In some embodiments, the prior therapy is gemcitabine monotherapy. In some embodiments, the prior therapy comprises the administration of gemcitabine and erlotinib. In some embodiments, the prior therapy comprises the administration of gemcitabine and capecitabine. In some embodiments, the prior therapy comprises the administration of gemcitabine and 5-FU. In some embodiments, the prior therapy comprises the administration of gemcitabine, erlotinib, capecitabine, and/or 5-FU. In some embodiments, the prior therapy is adjuvant

gemcitabine therapy. In some embodiments, the prior therapy is neoadjuvant gemcitabine therapy.

[0012] In some embodiments, the individual has progressed on the prior therapy at the time of treatment. For example, the individual has progressed within any of about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 months upon treatment with the prior therapy. In some embodiments, the individual is resistant or refractory to the prior therapy. In some embodiments, the individual has recurrent pancreatic cancer, i.e., the individual is initially responsive to the treatment with the prior therapy, but develops pancreatic cancer after about any of about 6, 7, 8, 9, 10, 11, 12, 24, or 36 months upon the cessation of the prior therapy.

[0013] Although the description below describes individuals who have progressed on a prior therapy (such as a gemcitabine-based therapy) as exemplary embodiments, it is understood that the description herein also applies to individuals who are resistant or refractory to the prior therapy, individuals who are unsuitable to continue with the prior therapy (for example due to failure to respond and/or due to toxicity), individuals who have recurrent pancreatic disease after the prior therapy, individuals who are non-responsive to the prior therapy, individuals who exhibit a less desirable degree of responsiveness and/or individuals who exhibit enhanced responsiveness. The methods and uses described herein include all second-line therapies for treating pancreatic cancers that involve the administration of a composition comprising nanoparticles comprising albumin and a taxane. The methods and uses described herein also include all third-line therapies for treating pancreatic cancers that involve the administration of a composition comprising nanoparticles comprising albumin and a taxane.

[0014] Thus, in some embodiments, there is provided a method of treating pancreatic cancer (such as advanced pancreatic cancer) in an individual in need thereof, comprising (or consisting of or consisting essentially of) administering to the individual an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin, wherein the individual has progressed on prior therapy (for example progressed after any of about 3, 6, 9, or 12 months upon initiation of the prior therapy). In some embodiments, the prior therapy is gemcitabine-based therapy, erlotinib-based therapy, or 5-FU-based therapy. In some embodiments, the method does not comprise

cancer is locally advanced pancreatic cancer, unresectable pancreatic cancer, or metastatic pancreatic ductal carcinoma. In some embodiments, the pancreatic cancer is resistant to the gemcitabine-based therapy. In some embodiments, the pancreatic cancer is refractory to the gemcitabine-based therapy.

[0028] The methods and uses described herein can be used for any one or more of the following purposes: alleviating one or more symptoms of pancreatic cancer, delaying progression of pancreatic cancer, shrinking pancreatic cancer tumor size, disrupting (such as destroying) pancreatic cancer stroma, inhibiting pancreatic cancer tumor growth, prolonging overall survival, prolonging disease-free survival, prolonging time to pancreatic cancer disease progression, preventing or delaying pancreatic cancer tumor metastasis, reducing (such as eradiating) preexisting pancreatic cancer tumor metastasis, reducing incidence or burden of preexisting pancreatic cancer tumor metastasis, preventing recurrence of pancreatic cancer, and/or improving clinical benefit of pancreatic cancer.

[0029] Also provided are compositions (such as pharmaceutical compositions), medicine, kits, and unit dosages useful for methods and uses described herein.

[0030] Provided herein are methods of treating pancreatic cancer in an individual in need thereof, comprising administering to the individual an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin, wherein the individual has progressed on a gemcitabine-based therapy. In some embodiments, the progression is within less than about 12 months. In some embodiments, the gemcitabine-based therapy further comprises erlotinib. In some embodiments, the gemcitabine-based therapy is monotherapy.

[0031] Provided herein are methods of treating resistant or refractory pancreatic cancer in an individual in need thereof, comprising administering to the individual an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin. In some embodiments, a prior therapy has stopped for at least 6 months when initiating administration to the individual of an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin. In some embodiments, the prior therapy is a gemcitabine-based therapy. In some embodiments, the

disclosed herein,, the exocrine pancreatic cancer is pancreatic ductal carcinoma. In any of the embodiments disclosed herein, the pancreatic cancer is locally advanced pancreatic cancer, unresectable pancreatic cancer, or metastatic pancreatic ductal carcinoma. In any of the embodiments disclosed herein, the composition comprising nanoparticles comprising taxane and albumin is administered parenterally. In any of the embodiments disclosed herein, the composition comprising nanoparticles comprising taxane and albumin is administered intravenously or intraarterially. In any of the embodiments disclosed herein, the taxane is paclitaxel. In any of the embodiments disclosed herein, the nanoparticles in the composition have an average diameter of no greater than about 200 nm. In any of the embodiments disclosed herein, the nanoparticles in the composition have an average diameter of less than about 200 nm. In any of the embodiments disclosed herein, the taxane in the nanoparticles are coated with albumin. In any of the embodiments disclosed herein, the individual is human. In any of the embodiments disclosed herein, levels of serum CA19-9 (carbohydrate antigen 19-9) in the individual are decreased by at least about 50% in comparison to the levels of serum CA19-9 prior to the treatment.

[0036] These and other aspects and advantages of the present disclosure will become apparent from the subsequent detailed description and the appended claims. It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present disclosure.

BRIEF DESCRIPTION OF FIGURES

[0037] Figure 1 shows early response in a target lesion of the baseline level and after 2 cycles of therapy with an albumin stabilized nanoparticle formulation of paclitaxel (i.e., *Nab*-paclitaxel).

[0038] Figure 2 is a Kaplan-Meier Survival Curves showing progression-free survival (Figure 2A) and overall survival (Figure 2B) after treatments with *Nab*-paclitaxel in Stages III and IV pancreatic cancer patients.

[0039] Figure 3 is a correlation between SPARC (Secreted Protein Rich in Cysteine) IHC (Immunohistochemsitry) and PFS (Progression-Free Survival). SD: Stable Disease; PR: Partial Response.

CLAIMS

We claim:

1. Use of a composition comprising nanoparticles comprising a taxane and an albumin in the manufacture of a medicament for treating pancreatic cancer in an individual in need thereof, wherein the individual has progressed on a gemcitabine-based therapy, wherein a prior therapy has stopped for at least 6 months when initiating administration of the medicament to the individual, and wherein the treatment is in combination with gemcitabine.

2. The use of claim 1, wherein the nanoparticle composition and gemcitabine are administered simultaneously or sequentially.

3. The use of claim 1, wherein the nanoparticle composition and gemcitabine are administered concurrently.

4. The use of any one of claims 1-3, wherein the gemcitabine-based therapy further comprises erlotinib.

5. The use of any one of claims 1-3, wherein the gemcitabine-based therapy is monotherapy.

6. The use of any one of claims 1-5, wherein the pancreatic cancer is exocrine pancreatic cancer or endocrine pancreatic cancer.

7. The use of claim 6, wherein the exocrine pancreatic cancer is pancreatic ductal carcinoma.

8. The use of any one of claims 1-7, wherein the pancreatic cancer is locally advanced pancreatic cancer, unresectable pancreatic cancer, metastatic pancreatic ductal carcinoma, refractory pancreatic cancer, resistant pancreatic cancer, or recurrent pancreatic cancer.

9. The use of any one of claims 1-8, wherein the composition comprising nanoparticles comprising taxane and albumin is administered parenterally.

10. The use of claim 9, wherein the composition comprising nanoparticles comprising taxane and albumin is administered intravenously or intraarterially.