great majority of cases, through the reactivation of the enzyme telomerase (Blackburn D.H., Nature, 408:53-56, 2000; Phatak, P. et al., Br. J. Pharmacol., 152: 1003-11, 2007 & Holt, S.E. et al., Nature Biotechnol., 14: 1734-1741, 1996). Telomerase is a ribonucleoprotein reverse transcriptase, which acts as the template for addition of new telomeric repeats, and the catalytic subunit hTERT (human telomerase reverse transcriptase). Telomerase permits cancer cells to overcome the fundamental limitations of infinite proliferation and renders them immortal. Thus, telomerase and telomeres have emerged as promising targets for anticancer therapies (Phatak, P. et al., Br. J. Pharmacol., 152: 1003-11, 2007, Chumsri, S. et al., Curr. Opin. Mol. Ther. 10: 323-333, 2008)

[0004] The major problem in developing effective and ultimately curative treatments for cancer lies in the fact that cancers are heterogeneous and contain mature cells as well as cells that are responsible for self-renewal, termed stem cells. Current cytotoxic anticancer agents are mainly aimed toward killing the mature cell population, but can not eradicate cancer stem cells. As a result, cancer often relapses and tumors then comprise more aggressive stem cell-like drug resistant cancer cells (Chumsri,S. et al., Curr. Opin. Mol. Ther. 10: 323-333, 2008). Therefore, there is a need for new therapeutic agents and/or regimens that can inhibit telomerase or target telomere to reduce or eliminate both mature and stem-like cancer cells including drug resistant cancer stem cells and mature cancer cells.

Summary

[0004a] In one aspect, the present disclosure refers to a use of sodium meta arsenite for manufacture of a pharmaceutical composition for use in combinatorial therapy for treatment of paclitaxel- or docitaxel- resistant forms of prostate cancer, wherein said pharmaceutical composition is to be administered in combination with paclitaxel or docetaxel.

[0005] In one example of the disclosure, there is provided a method for treating a refractive form of cancer in a patient. This is achieved by administering to the patient a therapeutically effective amount of sodium meta arsenite (NaAsO2 or KML001) alone or in combination with other anti-cancer agent(s). In certain examples, sodium meta arsenite is administered in a unit dose of 0.1 to 20 mg one or more times per day. In certain examples, the patient is monitored for the presence of a stem cell population following treatment with sodium meta arsenite. In certain other examples the patient may be so monitored for a period of up to four years or more following treatment with sodium meta arsenite. In certain examples the refractive cancer is prostate cancer, lung cancer, lymphoma or leukemia.

[0006] In another example of the disclosure, there is provided a method of treating a cancer patient who has a higher than normal serum level of IL-6 comprising administering to the patient a therapeutically effective amount of sodium met arsenite and monitoring the serum IL-6 level of the patient following a final sodium met arsenite treatment. Monitoring the patient's IL-6 level may be carried out periodically for up to four years or more following completion of sodium meta arsenite treatment.

[0007] In another example of the disclosure, there is provided a method of enhancing the efficacy of an anti-cancer agent in a patient suffering from a drug-resistant form of cancer comprising administering to the patient a therapeutically effective amount of sodium meta arsenite and an anti-cancer agent to which the cancer has been shown to be drug resistant.

[0008] In yet another example of the disclosure, there is provided a method of sensitizing refractive cancer cells in a patient to an anti-cancer agent to which the cancer cells were previously resistant comprising administering to the patient a therapeutically effective amount of each of sodium meta arsenite and the anti-cancer agent. The anti-cancer agent may be administered prior to administration of a sodium meta arsenite treatment regimen, after completion of a sodium meat arsenite treatment regimen or during administration of a sodium meta arsenite treatment regimen.

[0009] In yet another example of the disclosure, there is provided a method of inhibiting or preventing the recurrence of cancer in a patient. The method comprises administering to the patient a therapeutically effective amount of sodium meta arsenite following completion of a treatment regimen with one or more anti-cancer agents. In certain examples, the patient is monitored for the presence of a cancer stem cell population following treatment with sodium meta arsenite. Monitoring can be carried out periodically for up to four years or more.

[0010] Without being bound by a particular theory or mechanism, the reduction or elimination of a cancer stem cell population reduces or eliminates the cancer cell population produced by the cancer stem cell population, and thus reduces or eliminates the growth of a tumor, the bulk size of a tumor, the formation of a tumor and/or the formation of metastases. In other words, the reduction or elimination of the cancer stem cell population prevents the formation, reformation or growth of a tumor and/or metastases by cancer cells.

[0011] According to one example, the disclosure relates to a method of treating cancer comprising administering to a subject a therapeutically effective amount of sodium meta arsenite sufficient to reduce or eliminate drug resistant cancer stem cell population. In another example related to this aspect, the cancer stem cell population is resistant to paclitaxel. In yet another related example, the cancer stem cell population is resistant to docetaxel.

Brief Description of the Drawings

[0012] Figure 1A shows the detection of the side population (SP) in DU145wt and Doc50 resistant cells using Hoechst 33342 dye. Figure 1B shows the cell surface expression of Pgp in wt and resistant clones as determined by flow cytometry. White curves = PE (Phycoerythin)- isotype control stained cells and grey curves = Pgp positive cells. Figure 1C shows histograms for CD44 staining (grey curves) compared to isotype controls (white curves) in wt and taxane-resistant DU145 cells. Figure 1D shows growth curves comparing paclitaxel, docetaxel, and DU145wt cells when treated with docetaxel in a MTT assay. Figure 1E shows growth curves comparing paclitaxel, docetaxel and DU154wt cells when treated with KML001 in a MTT assay.

[0013] Figure 2A shows the side population of DU145wt cells stained with DCV dye. Figure 2B shows the side population of DU145wt treated with the BCRP/ABCG2 inhibitor Fumitremorgin C (FTC). Figure 2C. shows the side population of DU145wt treated with the Pgp/ABCB1 inhibitor Verapamil.

[0014] Figure 3A shows DU145wt treated with regular (control) media. Figure 3B shows DU145wt with pre-treated media containing KML at the IC100 concentration (13 μM) for 72 hours.

[0015] Figure 4A shows MTT proliferation assay showing DU145/ Pac200 treated with KML001. Figure 4B shows MTT assay proliferation showing DU145/ Pac200 treated with GRN163L.

[0016] Figure 5A shows the side population of DU145/ Pac200 cells treated with only DCV dye. Figure 5B shows the side population of DU145/ Pac200 treated with DCV and Fumitremorgin C (FTC). Figure 5C shows the side population of DU145/ Pac200 treated with DCV and verapamil. Figure 5D shows the side population assay showing

What is claimed is:

1. Use of sodium meta arsenite for manufacture of a pharmaceutical composition for use in combinatorial therapy for treatment of paclitaxel- or docitaxel- resistant forms of prostate cancer, wherein said pharmaceutical composition is to be administered in combination with paclitaxel or docitaxel.

2. Use according to claim 1 wherein the composition is formulated for oral administration.

3. Use according to claim 2 wherein the composition is formulated to deliver an amount of sodium meta arsenite in a dosage amount of from 0.1 to 20 mg/kg

4. Use according to claim 1 wherein the prostate cancer is resistant to paclitaxel.

5. Use according to claim 1 wherein the prostate cancer is resistant to docitaxel.