TREATING PANCREATIC CANCER AND NON-SMALL CELL LUNG CANCER WITH ATR INHIBIORS

BACKGROUND OF THE INVENTION

[0001] Pancreatic cancer is the tenth most common site of new cancers and is responsible for 6% of all cancer related deaths. The 5-year survival rate is less than 5%.

[0002] Current therapies involve either neoadjuvant treatment with chemotherapy (e.g., with gemcitabine) and / or radiation therapy or surgical removal followed by either adjuvant chemotherapy (e.g., with gemcitabine) or radiation therapy. Although the survival rate with treatment of gemcitabine increases the 5-year survival from 10% to 20%, there still is a strong need for better therapies for treating pancreatic cancer.

[0003] Several therapeutics have been tested in phase II and phase III trials though results have not been too promising. Tipifarnib, an oral farnesyltransferase inhibitor, did not show significant improvement in overall survival when combined with gemcitabine. Similarly, cetuximab, an epidermal growth factor receptor (EGRF), also showed no clinical benefit when combined with gemcitabine. Only a small increase in overall survival (6.24 months versus 5.91 months) was observed.

[0004] Lung cancer is the second most common form of cancer and is the leading cause of cancer-related mortality. Non-small cell lung cancer (NSCLC) is the most common form of lung cancer, accounting for about 85% of all lung cancer cases. Most patients present with advanced stage III or IV NSCLC with a 5-year survival of 24% and 4% respectively. Because of the advanced nature of disease on presentation, surgical resection is often not an option. For the majority of patients therapy involves chemotherapy and / or radiation treatment. The selection of chemotherapy is highly variable based on disease stage, patient performance criteria and geographical regional preference. In most cases chemotherapy is based on a doublet that includes a platinating agent such as Cisplatin or carboplatin and a second cytotoxic drug such as

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