Novel nanoparticle formulation of Sabizabulin (VERU-111) for pancreatic cancer treatment
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INTRODUCTION

• Pancreatic cancer (PanCa) is the fourth most common cause of death among both men and women in the US with an overall survival rate of just 5%.
• The management of PanCa, is exceptionally difficult due to the extremely poor response available therapeutic modalities.
• Microtubules are dynamic structures composed of α- and β-tubulin heterodimers that are required for many aspects of cellular functions, including mitosis. This has made them an attractive target for the development of anti-cancer agents.
• Aberrant expression of specific β-tubulin isotypes, particularly βIII-tubulin is important clinically in tumor aggressiveness and resistance to chemotherapy.
• VERU-111 (Fig. 1), an orally bioavailable, small molecule inhibitor has showed anti-cancer activity against a variety of cancers including pancreatic cancer.
• Herein, we have developed and characterized novel formulation of VERU-111 (MNP-VERU-111) which showed better potential therapeutic efficacy in vitro and ectopic xenograft mouse model.

METHODS

In vitro model systems: Pancreatic cancer cells (PanCa; AsPC1, and HPAFII).
MTS and colony formation assays: To investigate the effect of MNP-VERU-111 on cell proliferation and clonogenic potential of pancreatic cancer cells.
Invasion and Migration Assay: To investigate the effects of VERU-111 or MNP-VERU-111 on invasion and invasion using BD Matrigel-coated chambers wells, and invasion chamber for 24 hrs.
 Xenograft study: To investigate the effects of VERU-111 or MNP-VERU-111 on growth of pancreatic cancer cells xenograft-derived tumor in athymic nude mice.
 Flow cytometry: To investigate the effect of VERU-111 or MNP-VERU-111 on cell cycle and apoptosis analysis in pancreatic cancer cells.
 Western blot analysis: To investigate the effects of VERU-111 or MNP-VERU-111 on protein levels of β-tubulin isotypes in PanCa cells.
 Quantitative real-time PCR (qRT-PCR): To evaluate the mRNA expression of β-tubulin isotypes in PanCa cells.
 Immunohistochemistry: To determine the effect of VERU-111 or MNP-VERU-111 on β-tubulin isotypes in excised xenograft tumors.
 Confocal microscopy: To investigate the effect of VERU-111 or MNP-VERU-111 on the expression of β-tubulin isotypes in excised xenograft tumors.

REFERENCES


RESULTS

Generation and characterization of unique formulation (MNP-VERU-111) for pancreatic cancer treatment

MNP-VERU-111 more effectively inhibits β-tubulin isotypes in PanCa cells

MNP-VERU-111 restores the expression of miR-200c via targeting βIII-tubulin and ZEB1

MNP-VERU-111 more efficiently inhibits metastatic phenotype of PanCa cells

MNP-VERU-111 more efficiently inhibits the growth of pancreatic cancer cells-derived xenograft tumors

CONCLUSION

Our results demonstrate that MNP-VERU-111 is a new therapeutic modality which show more superior therapeutic efficacy than free VERU-111. We suggest that MNP-VERU-111 could be used as a new therapeutic modality for the treatment of pancreatic cancer alone or in combination with current therapeutic regimes.

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