BLACKSTONE
THERAPEUTICS

# CASE STUDY

## BST-103 and its Impact on Pancreatic Cancer Cell Lines

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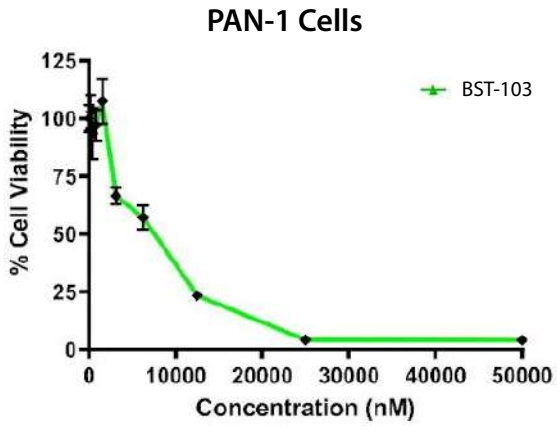
Despite recent advances in chemotherapy, pancreatic cancer remains a deadly disease and is the third leading cause of cancer related death in the United States[1] and by 2030, it will be second only to lung cancer. This is remarkable as it has Orphan Drug Designation, as there are approximately 56,000 new cases of pancreatic cancer diagnosed each year in the United States (2019, per the NCI). However, there are about 46,000 patient deaths, a disturbing fatality rate. Clinical studies on the utility of cannabinoids in the treatment of pancreatic cancer are lacking and urgently needed[2], [3]. With only small incremental gains, and a growing specificity of target (and therefore smaller patient target groups, some of whom may ultimately develop resistance), there is an urgent unmet need for broader, better and less toxic treatments for pancreatic cancer[4], [5]. Our group aims to exploit a remarkable property of a modified derivatives of rare cannabinoids that selectively disrupt the replication of pancreatic cancer cells[6].

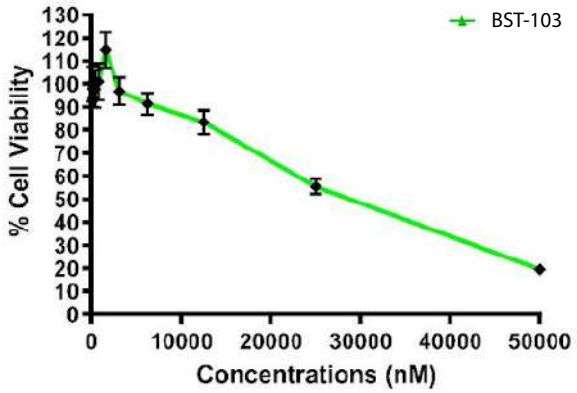
BST-103 was tested for its antineoplastic activity on the PDAC cells[6], which is the most common type of pancreatic cancer. Collaboration with the Karmanos Cancer Institute, led to pre-clinical in-vitro cell studies that generated data on the efficacy of BST-103 as a possible antineoplastic. The cell lines used were MIA-PaCa2, and PANC-1 cell lines. These cell lines are common endothelial cells that are associated and found in PDAC and are the target of many novel antineoplastics that are being researched currently which led us to test BST-103 on these cell lines. Below in Figure 1 is the graph on cell viability as well as the IC50 values generated. BST-103 generated in IC50 value of 5 µM on PANC-1 cell line and an IC50 value of 19.7 µM on the MIA-PaCa2 cell line.




| Compound | IC50 (µM) |
|---|---|
| BST-103 | 5.07 |

Figure 1: Comparison of effects of BST-103 on PANC-1

**MIA-PaCa2 Cells**

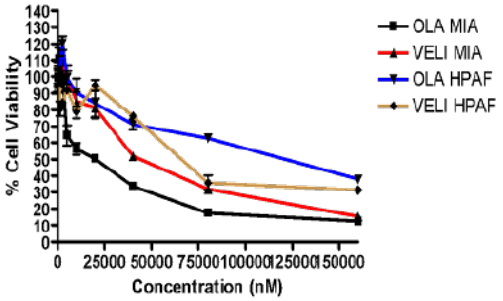



| Compound | IC50 (μM) |
|---|---|
| BST-103 | 5.07 |

Figure 2: Comparison of effects of BST-103 on MIA-PaCa2

Ongoing SAR studies with BST-103 are being conducted to reduce the IC50 value for better efficacy. For reference, PARP inhibitors were chosen as the comparison antineoplastic for the completion of data. PARP inhibitors are a class of compounds that inhibit the enzyme poly ADP ribose polymerase. PARP inhibitors are used in treatment of breast, ovarian, peritoneal, and fallopian cancer. PARP inhibitors are given as treatment to pancreatic cancer patients who have completed chemotherapy, to help support the treatment and reduce recurrence in pancreatic cancer. In Figure 3 is the IC50 values generated on the various cell lines.

**Comparison of Effects of PARP Inhibitors on Various Cell Lines**




| Cell Line | Compound | ICU (μM) |
|---|---|---|
| MIA-PaCa2 | Olaparib | 12.805 |
| MIA-PaCa2 | Veliparib | 35.04 |
| HPAF-II | Olaparib | 58.754 |
| HPAF-II | Veliparib | 75.112 |

Figure 3: Comparison of effects of PARP Inhibitors on various cell lines

**References**

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3. Malvezzi M, Bertuccio P, Rosso T, et al. European cancer mortality predictions for the year 2015: does lung cancer have the highest death rate in EU women? *Ann Oncol*. **2015**, 26, 779–786.

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5. Guzman M. Cannabinoids: potential anticancer agents. *Nat Rev Cancer.* **2003**, 3, 745–755.
6. Cruces, W., Ray, K. P., Jagtap, P. G., Patent Pending, 63/411,506, September 29, 2022