BLACKSTONE
THERAPEUTICS

CASE STUDY

BST-104 and its Impact on Pancreatic Cancer Cell Lines

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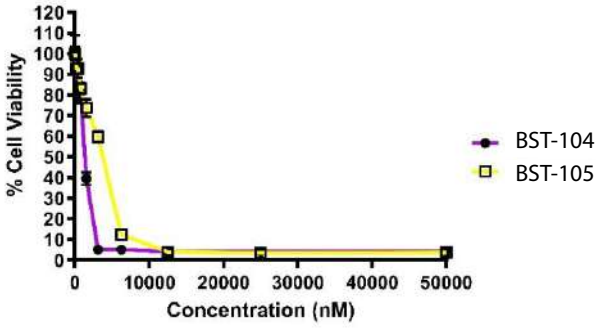
BST-104 is a compound currently being focused on for the direct treatment as an antineoplastic of pancreatic cancer. BST-104 was tested on PANC-1 and MIA-PaCa2 cell lines and showed low IC50 values which led to our first hit for drug modifications, shown in Figure 1. BST-104 has diastereomers which were purified and then tested individually on both cell lines. BST-111, and BST-112 had lower IC50 scores with their values at 5.29 and 8.02 μM respectively on the PANC-1 cell line.

PAN-1 Cells

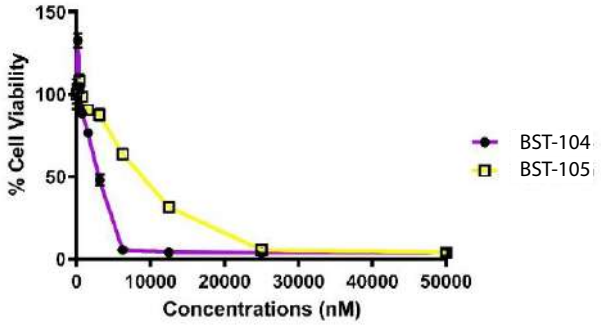


Compound	IC50 (μM)
BST-104	1.05
BST-105	2.55

Figure 1: Comparison of effects of BST-104 analogs on PANC-1

Shown in Figure 2, BST-104 tested on the MIA-PaCa2 cell line had a slight increase in the IC50 value but by marginal amounts as the compound is still highly effective.

MIA-PaCa2 Cells



Compound	IC50 (μM)
BST-104	1.3
BST-105	6.1

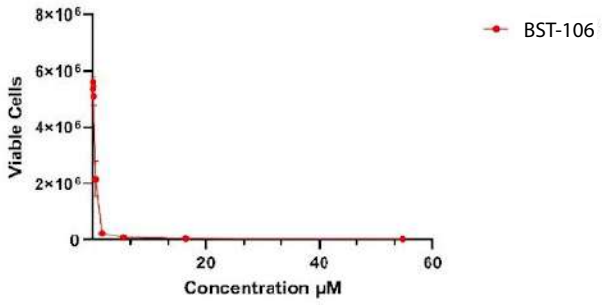
Figure 2: Comparison of effects of BST analogs on MIA-PaCa2

The value generated sits at 1.3 μM, marginal increase in the IC50 values, while the diastereomers of BST-104 had 3.24 μM for BST-111, and 4.77 μM for BST-112. The diastereomers were also tested on the AsPC-1 cell line with generally low IC50 values not making them great hits alone. BST-111 has a 4.85 μM value and BST-112 has a 6.17 μM value. Our group needs further SAR to increase the IC50 values for better results. Diastereomers

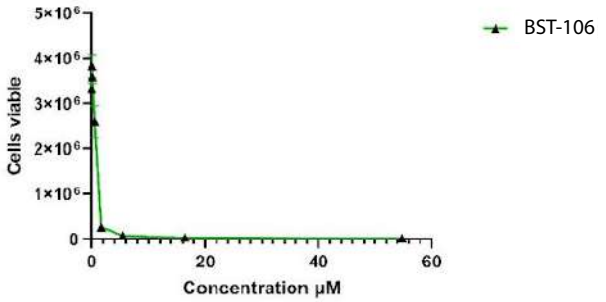
alone were not great, while BST-104 had better results towards the PDAC cell lines. Current antineoplastics, which are used to treat pancreatic cancer, have terrible IC50: cisplatin2 has 18.48 µM IC50 value on MIA-PaCa2 cell line as well as oxaliplatin2 with a 63.2 µM IC50 value. Below in Figure 3, the compound BST-106 has extremely well IC50 values in the pancreatic cell line meeting or even exceeding BST-104 IC50 capabilities. This can possibly be due to the flexibility and length of the functional group moieties as well as the scaffold that the compound has increased IC50 values.

Across the PDAC cell lines BST-106 has almost reached the nano-molar range in which only possible slight modifications can be made to increase, through the data as a single compound BST-106 is possible to be used single handedly or formulated for more targeted delivery to the pancreas for more direct treatment.

MIA-PaCa2 Cells



PAN-1 Cells



AsPC-1	MiaPaCA-2	PANC-1
1.05	0.53	0.79

Figure 3: Impact of BST-106 MIA-PaCa2 and PANC-1 cell lines

References

1. Cruces, W., Ray, K. P., Jagtap, P. G., Patent Pending, 63/411,506, September 29, 2022
2. Yang, W.; Soares, J.; Greninger, P.; Edelman, E. J.; Lightfoot, H.; Forbes, S.; Bindal, N.; Beare, D.; Smith, J. A.; Thompson, I. R.; Ramaswamy, S.; Futreal, P. A.; Haber, D. A.; Stratton, M. R.; Benes, C.; McDermott, U.; Garnett, M. J. Genomics of Drug Sensitivity in Cancer (GDSC): A Resource for Therapeutic Biomarker Discovery in Cancer Cells. Nucleic Acids Res. 2013, 41 (Database issue), D955-61. https://doi.org/10.1093/nar/gks1111.