The potent quadruplex-binding compound QN-302 shows anti-tumor activity as a monotherapy in an orthotopic in vivo model of pancreatic cancer

Abstract #6240

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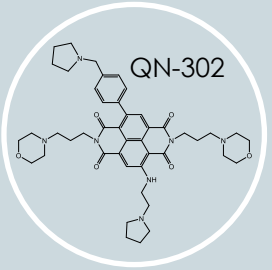
- **QN-302** is a tetra-substituted naphthalene diimide derivative (Ahmed et al, 2020)
- Has high potency, targets quadruplex (G4) sequences in the promoter regions of cancer genes
- low nM anti-proliferative activity in a panel of human pancreatic cancer (PDAC) cell lines
- Significant anti-tumor activity in xenograft and genetic (KPC) models of PDAC

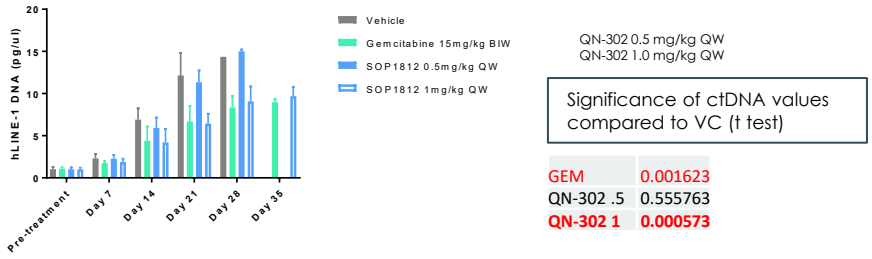
PDAC cell line	IC_{50} 96 hr (nM)
Mia-Paca2	1.3
PANC-1	1.4
CAPAN-1	5.9
Bx-PC3	2.6



BxPC-3 cells - derived from a 61 years old female with a primary pancreatic adenocarcinoma, lack a KRAS mutation.
Cells were orthotopically implanted into the pancreas of female athymic nude mice. 7 days after implants, imaging done (IVIS) to confirm tumor take. Treatment was continued for up to 3 weeks with weekly imaging to quantify efficacy. At the end of the treatment period, tumor tissue/pancreas was removed and weighed. 10 animals per treatment group to ensure sufficient animals were successfully implanted. Animals dosed with 1 x weekly IV QN-302 at 0.5 and 1.0 mg/kg, over 21 days. A separate group was treated with gemcitabine twice weekly IV during this period, at 15 mg/kg. Blood samples from animals were collected on a weekly basis and were used to detect & quantify circulating tumor DNA as a method of following drug efficacy.

In line with previous studies QN-302 was well-tolerated at 0.5 and 1 mg/kg QW with no adverse effects on animal health or behavior noted during the study.
Efficacy was observed in animals treated with gemcitabine or QN-302 at 1 mg/kg QW:
Circulating tumor DNA levels were significantly less than vehicle controls in gemcitabine-treated animals from day 7 and QN-302 1 mg/kg treated animals from day 14 of treatment. Survival was significantly increased in gemcitabine and QN-302 1 mg/kg QW treatment groups.
In gemcitabine and QN-302 1 mg/kg QW treated groups, the weight of pancreas tissue was significantly less than vehicle controls.

cTDNA levels quantified by QPCR amplification of LINE-1 sequences (a repetitive sequence in the human genome with ~100,000 elements) in whole blood from mice treated with QN-302 or gemcitabine.

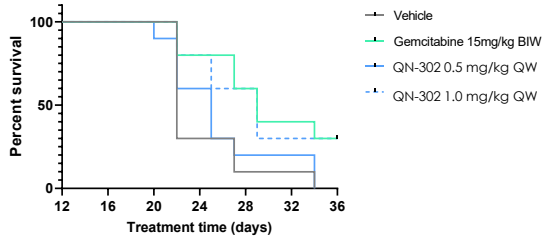


QN-302 0.5 mg/kg QW
QN-302 1.0 mg/kg QW

Significance of ctDNA values compared to VC (t test)

GEM	0.001623
QN-302 .5	0.555763
QN-302 1	0.000573

Survival plots of mice dosed with QN-302 or gemcitabine. Plots from both groups were significantly different from vehicle controls (p=0.0141 and 0.0219, respectively; Log Rank (Mantel-Cox) Test).



This orthotopic study is the 4th *in vivo* pancreatic cancer model that shows anticancer activity for QN-302, further confirming its potential for human cancer treatment. QN-302 is bio-available and well tolerated at therapeutic doses. It is being developed for clinical evaluation by Qualigen Therapeutics Inc and is currently undergoing GLP toxicity evaluation prior to IND submission. It was granted Orphan Drug status for PDAC by the FDA in Jan 2023