

M402, a Novel Drug Candidate for Pancreatic Cancer: Efficacy in Animal Models and Initial Clinical Study Design

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Background

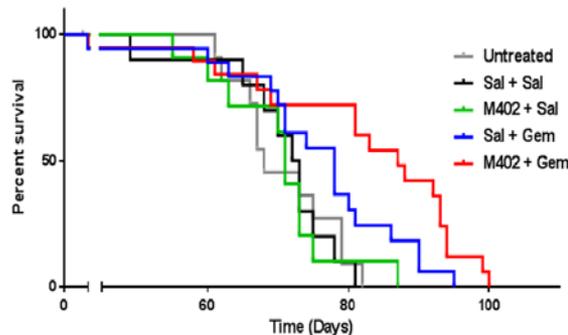
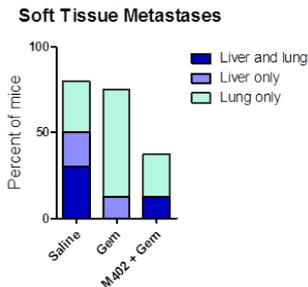
- M402's development is based on nonclinical studies showing heparins impacting pathways related to the pathogenesis of cancer as well as decades of reports of antitumor activity of heparins in cancer patients. Because the dose of these medicines has been limited by their anticoagulant activity, M402 – derived from unfractionated heparin – has been designed to have significantly reduced anticoagulant activity while optimizing heparin's antitumor properties.
- Nonclinical data showed potent binding of M402 to multiple growth factors, adhesion molecules, and chemokines to inhibit tumor progression, metastasis, and angiogenesis. Results from two models of pancreatic cancer are presented.

Methods

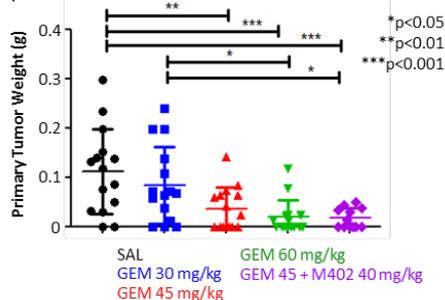
- Genetic Model:** The *Kras*^{G12D/+}*p53*^{R172H/flox}*pDxCre* transgenic mouse spontaneously develops pancreatic tumors by Day 40. Metastasis to LN, liver, spleen, and lung. Considered one of the most physiologically relevant models of pancreatic cancer. Starting on Day 30: M402 or saline (SAL) via minipump, or gemcitabine (GEM) 50 mg/kg, q3d or SAL.
- Capan-2** cells implanted into pancreas on Day 0; M402 40 mg/kg/day via osmotic pump starting on Wk 1 or 5; GEM at 30, 45, 60 mg/kg twice weekly starting on Day 28.

Results

- Genetic Model Results:** M402 + GEM offered a survival benefit over GEM (right) and reduced the metastatic rate (below).



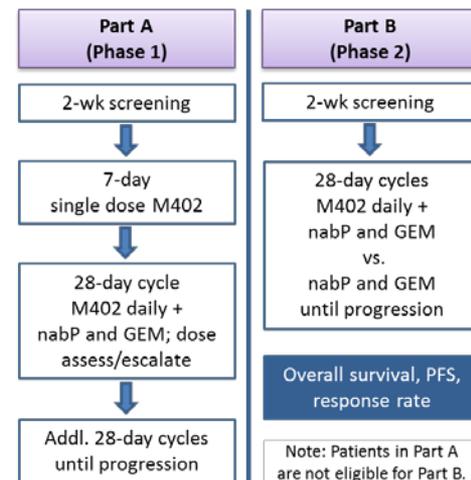
- Capan-2 Results:** M402 reduced tumor growth as monotherapy and when combined with GEM (below).



Phase 1/2 Study

- Part A is a first-in-human, open-label, multiple ascending dose study in patients with metastatic pancreatic cancer. Part A objectives: to evaluate the safety and tolerability of M402 in combination with Abraxane® (nab-paclitaxel; nabP) and GEM and to establish the dose of M402 to take forward in Part B.
- Part B will be a randomized, controlled study investigating the antitumor activity of M402 + nabP + GEM versus nabP + GEM.
- Part A is ongoing, with several dose cohorts completed.
- Full Part A data are expected 1H 2014.

Phase 1/2 Study (cont.)



Conclusions

- These and other promising data from in vitro and in vivo experiments support M402's evaluation in the ongoing clinical study.
- M402's broad mechanism of action may also support the future clinical investigation of M402 in a variety of other cancers.