M402, a Heparan Sulfate Mimetic and Novel Candidate for the Treatment of Pancreatic Cancer

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PHASE 1/2 STUDY DESIGN

Design of First-in-Human Clinical Study with M402

Part A is an open-label, multiple ascending dose study, in patients with metastatic pancreatic cancer. The objectives of Part A are to establish tolerability and pharmacokinetic profile of escalating M402 doses in combination with gemcitabine in patients with metastatic pancreatic cancer.

Part B is a randomized, controlled phase investigating the antitumor activity of M402 in combination with gemcitabine versus gemcitabine alone in the same patient population.

RESULTS

M402 Prolongs Survival and Inhibits EMT and Metastasis in a Genetically Engineered Model

A. M402 monotherapy started either Week 1 or 5, testing different doses of M402 (10-40 mg/kg/day). B. Gemcitabine or Gemcitabine + M402 commenced on the same day, with an escalating dose of M402 (40 + 45 mg/kg) combined with a fixed dose of Gemcitabine (40 mg/kg). C. Tumor Weight [g]

M402 Reduces Tumor Growth and SHH Signaling in the Orthotopic Capan-2 Model

A. Monotherapy Primary Tumor Weights

B. Combination Therapy Primary Tumor Weights

C. Individual data, mean and SD

D. Individual data, mean and SD

PHASE 1/2 STUDY DESIGN

CONCLUSIONS

• M402 modulated tumor-stroma interactions involved in metastatic and desmoplastic pathways in two pancreatic cancer models.

• In the genetically engineered mouse model:

  • M402 in combination with gemcitabine prolonged survival, decreased metastases and local invasion, and inhibited epithelial–mesenchymal transition.

• In the orthotopic Capan-2 pancreatic cancer model:

  • M402 monotherapy showed a dose-dependent reduction in primary tumor weight, while M402 in combination with gemcitabine almost completely inhibited primary and metastatic tumor growth, which may be related to M402’s effect on SHH signaling.

• These results provide a rationale for investigating the clinical use of M402. A first-in-human study has been initiated that will evaluate the safety, pharmacokinetics, efficacy, and biomarker profiles of escalating M402 doses in combination with gemcitabine in patients with metastatic pancreatic cancer.

• M402 can inhibit angiogenesis, tumor progression and metastasis in animal models by modulating a variety of polysaccharide-based binding proteins, which may support the clinical investigation of M402 in a range of cancers.