Inhibition of tumor growth and post-treatment regrowth by SM08502, a novel, small-molecule CDC-like kinase (CLK) inhibitor, in combination with standard of care in pancreatic cancer models

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Background

• Relapse and treatment resistance remain common in pancreatic cancer (PC) with standard of care (SOC) chemotherapy regimens
• Combining SOC with targeted drug therapies may improve treatment outcomes and clinical benefits

Results

• Oral SM08502 potently inhibited tumor growth both alone and in combination with chemotherapy
• The combination of SM08502 with GEM/P or GEM/Nab-P inhibited tumor growth more strongly than either treatment alone
• SM08502 extended antitumor effects into the post-treatment period when combined with SOC in genetically distinct PC models
• Improved survival and delay in tumor regrowth after treatment cessation suggest that SM08502 could help maintain treatment response in PC
• SM08502 was generally well tolerated

These data showed that the combined application of SM08502 with SOC therapy has the potential to provide clinical benefit in PC

• A Phase 1 study assessing the safety, tolerability, and pharmacokinetics of SM08502 in subjects with advanced solid tumors is ongoing (NCT03355066)

Methods

• Cell line-derived xenograft – Nude mice were implanted subcutaneously in the right flank with Capan-1 or HPAFII PC-derived cell lines then randomized to treatment and vehicle (control) groups when tumors reached ~100-200 mm³ (Figs. 1-3)
• Patient-derived xenograft (PDX) model – Severe combined immunodeficient (SCID) mice were implanted subcutaneously in both flanks with a patient-derived tumor (PNX0001, NexsusPharma, Inc) fragment and randomized; tumor growth was calculated as percent relative to size at implantation (Fig. 4)
• Tumor growth inhibition (TGI) was calculated relative to the vehicle control group (treatment phase) or the corresponding SOC group (observation phase)

Figure 1. SM08502 + GEM inhibited tumor growth in Capan-1 xenografts

• Tumor regressions were assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) guidelines: 30-100% reduction in tumor volume relative to the start of the study. Safety and tolerability were assessed by bodyweight measurement

Figure 2. SM08502 + GEM/P inhibited tumor growth and induced tumor regression HPAFII xenografts

Conclusions

• Inhibition of tumor growth and post-treatment regrowth by SM08502, a novel, small-molecule CDC-like kinase (CLK) inhibitor, in combination with standard of care in pancreatic cancer models

Figure 3. SM08502 + GEM/Nab-P delayed tumor regrowth and improved survival in Capan-1 xenografts

Figure 4. SM08502 + GEM/Nab-P inhibited tumor regrowth in a PDX model

References

9. All authors are employees, shareholders, or consultants of Samumed, LLC.

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