A phase 1 safety study of SBP-101, a polyamine metabolic inhibitor, for pancreatic ductal adenocarcinoma (PDA).

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Abstract Disclosures

Abstract:
Background: SBP-101 (diethyl dihydroxyhomospermine), a polyamine (PA) analogue of spermine, inhibited growth in 6 human PDA cell lines and 3 murine xenograft tumor models. A Phase 1 dose escalation study assessed the safety, tolerability and pharmacokinetics (PK) of SBP-101 in previously treated patients with locally advanced or metastatic PDA. **Methods:** In a modified 3x3 dose escalation scheme, daily subcutaneous injections of SBP-101 were dosed at 0.05, 0.1, 0.2, 0.4 or 0.8 mg/kg, Monday-Friday for 3 weeks, followed by 5 weeks of observation (1cycle), for 1 or 2 cycles. Safety and tolerability were evaluated by clinical and laboratory assessments. PK was evaluated on Days 1 and 18 of cycle 1. Efficacy was assessed by RECIST criteria and overall survival. **Results:** Twenty-nine patients were enrolled in 5 cohorts: (1: N = 3; 2: N = 5; 3: N = 4; 4: N = 7; 5: N = 10). Twenty-six had ≥2 prior chemotherapy regimens. Drug-related toxicity in cohorts 1-4 was minimal, although one patient in cohort 4 developed focal pancreatitis at the site of the tumor at 2.3 months. Most common adverse events (AEs) were abdominal pain, constipation, decreased appetite, dehydration, diarrhea, fatigue, nausea and vomiting. Most were grades 1 or 2 or considered unlikely or not related. No drug-related bone marrow suppression or peripheral neuropathy was seen at any dose. No DLTs occurred in cohorts 1-4. Three patients in cohort 5 developed serious adverse events considered dose limiting toxicities: bacterial sepsis with metabolic acidosis (N = 1), hepatic and renal failure with elevated lipase (N = 1) and superior mesenteric vein thrombosis with metabolic acidosis (N = 1). Plasma C_{max} and $AUC_{0\text{-}t}$ increased linearly with dose. Stable disease occurred in 2 patients each in cohorts 3 and 4, and in 4 patients in cohort 5. Median survival in cohort 3 was 5.9 months. **Conclusions:** SBP-101 was well tolerated in this study at dose levels 1-4; 0.8 mg/kg exceeded the maximum tolerated dose (MTD). Best tumor response and survival occurred with 0.2 mg/kg/day. The low incidence of AEs below the MTD and absence of bone marrow toxicity or peripheral neuropathy suggest the potential for SBP-101 as an addition to front line treatment for PDA and justify a combination study. Clinical trial information: NCT02657330