SBP-101, a Polyamine Metabolic Inhibitor, Administered in Combination with Gemcitabine and Nab-paclitaxel, Shows Signals of Efficacy as First-Line Treatment for Subjects with Metastatic Pancreatic Ductal Adenocarcinoma

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Background: SBP-101, a polyamine metabolic inhibitor, achieved growth inhibition in 6 human pancreatic ductal adenocarcinoma (PDAC) cell lines and a mouse xenograft tumor model of human PDAC. SBP-101 monotherapy in heavily pretreated patients showed a median survival of 5.9 months at the optimal dose level. The purpose of the present study was to assess the safety, tolerability, PK, and efficacy of SBP-101 in combination with gemcitabine (G) and nab-paclitaxel (A) in patients with previously untreated metastatic PDAC.

Methods: In a modified 3+3 dose escalation scheme, subcutaneous injections of SBP-101 were administered at 0.2, 0.4 or 0.6 mg/kg on days 1, 8, 15 of each cycle. G (1000 mg/m2) and A (100 mg/m2) were administered intravenously on Days 1, 8 and 15 of each cycle. Safety and tolerability were evaluated by clinical and laboratory assessments. PK was evaluated on day 1 of cycle 4. All patients were treated with calcium carbonate for proton suppression due to lack of PK samples in cohort 1 were below the limits of detection at most time points, but plasma Neutropenia typically seen with G+A alone. ORR (62%) and DCR (85%) exceeded the historical rates reported for FOLFIRINOX (62%, 70%) in pivotal trials; responses were accompanied by large decreases in CA 19.9 levels. Signals of early efficacy support continued development of SBP-101 as an addition to combination first-line therapy for PDAC.

Results

As of January 4, 2020, the response–evaluable subjects in cohorts 2 and 3 (N=13) had a CA-19-9 maximum decrease greater than 50%; No Dose

Conclusions

SBP-101 was well-tolerated when administered at doses tested in combination with G/A in subjects with previously untreated metastatic pancreatic adenocarcinoma. Treatment-related liver function abnormalities were mostly asymptomatic and reversed when SBP-101 was interrupted and doses restored. There was no evidence that SBP-101 potentiates the Grade 3 hematologic events or peripheral neuropathy typically seen with G+A. ORR (62%) and DOR (35%) exceeded the historical rates reported for FOLFIRINOX (62%, 70%) in pivotal trials; responses were accompanied by large decreases in CA-19-9. Signals of early efficacy support continued development of SBP-101 as an addition to combination first-line therapy for advanced PDAC and as neo-adjuvant treatment for patients with potentially resectable disease.

Sources: Von Hoff 2013, Conroy 2011

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