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

N. Singh1, D. Sigal2, N.C. Tebbit3, A.F. Here2, A. Nagrial4, S. Lumba5, T. George6, S.L. Smith7, S. Gagnon8, M.J. Walker9, M.T. Cullen10

1Fitzherbert Cancer Centre, Kurralta Park, SA, and University of Adelaide, SA, Australia; 2Syncoma Clinic and Sir Louis NI Anderson Cancer Centre, San Diego, CA, USA; 3Ohio State Johnnie Cancer, Wellness and Research Centre, Austin Health, Heidelberg, VIC, Australia; 4University of Rochester Medical Center, Rochester, NY, USA; 5Blackbird Hospital Cancer and Hematology Centre, Blackwood, NSW, Australia; 6Oletha Private Hospital, Toorak, VIC, Australia; 7University of Florida, Gainesville, FL, USA; 8Caurace Oncology, Excelsior, MN, USA; 9Medion Therapeutics, Inc, Minneapolis, MN, USA


Purpose: To assess the PK, safety and efficacy of SBP-101 in combination with gemcitabine (G) and nab-paclitaxel (A) in patients with metastatic unresectable metastatic PDAC (M1c).

Methods: This multicenter, open-label, randomized, multi-arm, dose-escalation Phase I/II study investigated SBP-101 in combination with G (800 mg/m2, every 3 weeks) and A (125 mg/m2, every 3 weeks) administered as a 30 min infusion every 3 weeks. Patients were randomized to receive 4 cohorts of 6 patients each: Cohort 1-3 received 9, 10, or 11 mg/kg SBP-101, respectively, on day 1 of each cycle, and Cohort 4 received a 4 mg/kg dose. Dose escalation steps in Cohorts 1-3 were 1 mg/kg SBP-101 and in Cohort 4, 2 mg/kg. Safety assessments were done up to day 14 of each cycle. Dose modification or dose reductions were allowed up to 100% of the original dose on the basis of safety and efficacy. Pharmacokinetics was done in Cohort 3 and Cohort 4. AEs were graded using the NCI-CTC v4.0 classification; AEs were classified as definitely, probably or possibly related and not related events as unlikely or probable.

Results: A total of 50 patients were randomized into Cohort 1-4: SBP-101; G (N=10), A (N=10), G+A (N=10) and G+A (N=10). Related adverse events (AEs) were defined as AEs considered definitely, probably or possibly related and not related events as unlikely or probable. The most common Grade ≥3 AEs related to any study medication were neutropenia in 13 (26%) patients and neutropenic fever in 5 (10%) patients. Grade 3/4 neutropenia occurred in 10 patients (20%), Grade 3/4 febrile neutropenia in 6 (12%) patients. One patient experienced Grade 3 diarrhea, 1 patient each experienced Grade 3 fatigue and Grade 3 dehydration. The treatment-related events related to all 3 arms at baseline were dehydration (N=7), fatigue (N=6), nausea (N=6), vomiting (N=5), diarrhea (N=4), and neutropenia (N=4). The most common Grade ≥3 AEs related to SBP-101 were neutropenia (N=6) and neutropenic fever (N=2). Fatigue was the most common Grade ≥3 AE related to G (N=3) and A (N=3). The objective response rate (ORR) for SBP-101 was 48% (95% CI 29-71%) and disease control rate (DCR) was 70% (95% CI 52-86%). The ORR for G+A was 23% (95% CI 7-46%) and DCR was 48% (95% CI 28-67%). Median PFS for SBP-101, G+A, and historical data on G+A was 4.0 months (95% CI 2.4-6.8), 4.5 months (95% CI 2.2-5.9), and 4.0 months (95% CI 2.5-5.1), respectively. Median OS for SBP-101, G+A, and historical data on G+A was 9.4 months (95% CI 7.4-12.0), 9.9 months (95% CI 7.4-12.0), and 9.4 months (95% CI 7.4-12.0), respectively. Nine patients were assessable for pharmacokinetics. The mean plasma concentration of SBP-101 increased linearly with SBP-101 dose. The area under the curve (AUC) was positively correlated with dose and the elimination half-life was 7.9 hours (95% CI 5.9-10.0).

Conclusions: SBP-101 was well-tolerated when administered at doses and schedules tested in combination with G and A in patients with previously untreated metastatic pancreatic adenocarcinoma. Treatment-related liver function abnormalities were seen in the subjects who were subsequently managed with SBP-101 dose reduction in Phase 1. There was no evidence that SBP-101 potentiates the Grade 3 hemorrhagic events or peripheral neuropathy typically seen with G and A. Source: ASCO 2021 Abstract 4127


table

Figure 1B. Best Tumor Response per Subject – Cohort 2 + Phase 1b. Subject 2 (21.5 months). One patient did not have a post-baseline scan with RECIST tumor assessment.

In the responsive-evaluable subjects in Cohort 4 + Phase 4 + Phase 1b, 11 had treatment with SBP-101. The SBP-101 objective response rate (ORR) was 77%, and the DCR was 100% by RECIST criteria (SD or better for ≥ 18 weeks). Median PFS in Cohort 2 was 5.3 months and median OS was 10.3 months compared with ORR of 48%, DCR of 70%, PFS of 5.2 months and median OS (not yet reached) in Cohort 4 + 1b.

Conclusions: SBP-101 was well-tolerated when administered at doses and schedules tested in combination with G and A in subjects with previously untreated metastatic pancreatic adenocarcinoma. In the responsive-evaluable subjects in Cohort 4 + Phase 4 + Phase 1b, 11 had treatment with SBP-101. The SBP-101 objective response rate (ORR) was 77%, and the DCR was 100% by RECIST criteria (SD or better for ≥ 18 weeks). Median PFS in Cohort 2 was 5.3 months and median OS was 10.3 months compared with ORR of 48%, DCR of 70%, PFS of 5.2 months and median OS (not yet reached) in Cohort 4 + 1b.

Conclusions: SBP-101 was well-tolerated when administered at doses and schedules tested in combination with G and A in subjects with previously untreated metastatic pancreatic adenocarcinoma. Treatment-related liver function abnormalities were seen in the subjects who were subsequently managed with SBP-101 dose reduction in Phase 1. There was no evidence that SBP-101 potentiates the Grade 3 hemorrhagic events or peripheral neuropathy typically seen with G and A. Source: ASCO 2021 Abstract 4127


table

Figure 1A. Best Tumor Response per Subject – Cohort 2 + Phase 1b. Subject 1 (21.5 months). One patient did not have a post-baseline scan with RECIST tumor assessment.

Figure 1B. Best Tumor Response per Subject – Cohort 4 + Phase 1b. Subject 7 (8.0 months). One patient did not have a post-baseline scan with RECIST tumor assessment.

In the responsive-evaluable subjects in Cohort 4 + Phase 4 + Phase 1b, 11 had treatment with SBP-101. The SBP-101 objective response rate (ORR) was 77%, and the DCR was 100% by RECIST criteria (SD or better for ≥ 18 weeks). Median PFS in Cohort 2 was 5.3 months and median OS was 10.3 months compared with ORR of 48%, DCR of 70%, PFS of 5.2 months and median OS (not yet reached) in Cohort 4 + 1b.

Conclusions: SBP-101 was well-tolerated when administered at doses and schedules tested in combination with G and A in subjects with previously untreated metastatic pancreatic adenocarcinoma. Treatment-related liver function abnormalities were seen in the subjects who were subsequently managed with SBP-101 dose reduction in Phase 1. There was no evidence that SBP-101 potentiates the Grade 3 hemorrhagic events or peripheral neuropathy typically seen with G and A. Source: ASCO 2021 Abstract 4127


table