Phase II Trial of SM-88 in Patients with Metastatic Pancreatic Cancer: Preliminary Results of the 1st Stage

Marcus Smith Noel, Andrew Wang-Cilliman, Alyson J. Ocean, Sant Chethal, Giuseppe Del Principe, Vincent J. Pizzocro, University of Rochester Wilmot Cancer Institute, Rochester, NY; Washington University, St. Louis, MO; Cornell Medical College, NY, NY; Sarcora Oncology Center, Santa Monica, CA; Tyne Technologies, Inc., NY, NY; Virginia Mason Medical Center, Seattle, WA.

BACKGROUND

Pancreatic cancer remains a clinically challenging disease with an 85% mortality rate within 12 months of initial diagnosis (ACS Fact Sheet). Recent clinical trials have shown median overall survival (OS) for four to six months with single-agent RECIST response rates in the second-line setting (Conroy et al. 2011; NAPOLI-2).

The standard of care remains toxic chemotherapy regimens (FOLFIRINOX or gemcitabine with nab-paclitaxel) with grade 3 or greater toxicity in over 50%.

Currently, there are no FDA approved treatments specifically indicated for metastatic pancreatic adenocarcinoma patients. Neither ASCO nor NCCN guidelines recommend any treatment for metastatic pancreatic cancer patients.

SM-88 is a novel anticancer regimen that consists of one investigational agent (L-3,4-dihydroxyphenylalanine, DOPA methyl ester, SM88) and two investigational drugs (mesna, anuric, and oxacillin).

It is hypothesized that, including both the DOPA and mesna contribute to the anticancer properties of SM88. Both DOPA and mesna are believed to be drug-specific interactions with mechanisms of action.

TRIAL DESIGN

Tyne-Me-Panc (NCT 03127175) is a 2 Part randomized, open label Phase II of SM-88 in previously treated metastatic pancreatic adenocarcinoma patients who have failed chemotherapy, and an Eastern Cooperative Oncology Group (ECOG) score of 2.

Part I: Subjects were randomized to receive either one of two dosing regimens for 21 days of treatment: 450 mg QID or 600 mg BID.

The trial dosed methotrexate (15 mg SQ), prednisone (10 mg QD), and oxacillin (500 mg QD), with the same regimens of nondiuranic and oxacillin.

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The present study describes the efficacy results from randomized Part I of Tyne-Me-Panc.

Methods data are presented on pooled data (0.2 mg GSR) at sm-88.org. Cutoff 37, 2019 Abstract 4 (Feb 27)

Additional safety data is on protocol ID 8 (Cullinane 2019, suppl. 8th 310)

SAFETY

Survival status is ongoing but reported here only as of Dec 31, 2019. All patients were analyzed using standard methods. Subjects were censored if they did not follow up for any reason.

CT imaging was performed at baseline and repeated every other cycle.

The response was determined according to RECIST 1.1 by BRST and the local investigator separately.

Safety monitoring for this trial was conducted in accordance with CTCAE toxicity criteria.

At baseline, patients were classified by the three major toxic effects at baseline, and at the end of each cycle.

ENROLLMENT & EVALUATIVE SUBJECTS

46 patients were screened for enrollment and 39 met criteria for randomization.

18 subjects did not complete any cycle due to grade 3 or 4 neutropenia (range 7 + 26 days total treatment) and were assigned to subsequent antibody or placebo.

The present analysis includes data from the 39 evaluable subjects unless otherwise stated.

RESULTS

As of Jan 4th, 2019, 75% (7/9) of evaluable subjects remained at a median follow up of 4.2 months (range 1.2 - 8.6 months).

No subjects were lost to follow up.

A detailed description of the Phase II safety data can be found on our website at CUC GSR 1.2019 (Smith Noel et al. 2019). There were limited grade 4 metabolic changes, which were significant of the treatment.

CONCLUSIONS

95% of subjects were alive at a median of 4.2 months follow up.

Among the 18 subjects who did not complete any cycle due to grade 3 or 4 neutropenia, a subset of 10 subjects underwent a total of 27 cycles (1-7 weeks, 1 cycle median) with no grade 3 or 4 neutropenia observed.

There were limited grade 4 metabolic changes, which were significant of the treatment.

REFERENCES


Corresponding Author: (a) Giuseppe T. Pizzocro (TyneKore) (b) +1-877-343-0616