

CPI-613 enhances FOLFIRINOX response rate in stage IV pancreatic cancer

A.T. Alistar¹, R. Desnoyers¹, R.J. D'Agostino², B. Pasche¹

¹*Hematology Oncology, Wake Forest University Comprehensive Cancer Center, Winston Salem, NC, USA,*

²*Biostatistical Sciences, Wake Forest University*

Comprehensive Cancer Center, Winston Salem, NC, USA

Background: Pancreatic cancer has a current five-year survival rates of less than 10%. Current standard treatment is combination chemotherapy with FOLFIRINOX or Gemcitabine + Abraxane. The glycolic and mitochondrial metabolism is aberrant in pancreatic cancer and translates into chemo-resistance. Inhibition of glutamine metabolism can potentially synergize with therapies that increase intracellular reactive oxygen species such as chemotherapy. The lipoate derivative CPI-613 is a first-in-class agent that targets mitochondrial metabolism. Whether this novel anti-cancer agent could enhance the efficacy of FOLFIRINOX is unknown.

Methods: This phase 1 study employed a two-stage dose-escalation schema to determine the maximum-tolerated dose (MTD) and safety of CPI-613 when used in combination with modified FOLFIRINOX in patients with metastatic pancreatic adenocarcinoma. Efficacy was assessed through response rates and estimates of progression-free (PFS) and overall survival (OS).

Results: The maximum-tolerated dose (MTD) was 1000 mg/m². The treatment was well tolerated, establishing that a reduced dose FOLFIRINOX combination with CPI-613 is feasible. Among the 18 patients enrolled at the MTD, there were 3 (16.6%) patients with a complete response (CR), 9 with a partial response (PR), 2 with stable disease and 4 with progressive disease. The PR + CR rate was 67% with a 95% Clopper-Pearson (exact) confidence interval of 41% to 87%. As follow-up is ongoing, estimates of PFS and OS are still immature, with current median PFS estimated as at least 186 days and median OS estimated as at least 268 days to date. Conclusions: CPI-613 is a first in class non redox active lipoate derivative being tested in phase I clinical trial in combination with FOLFIRINOX. The response rate was 67%, which is more than twice higher than FOLFIRINOX (32%). The CR rate is also higher than FOLFIRINOX. This novel combination therapy may emerge as the most effective treatment for patients with stage IV adenocarcinoma of the pancreas as response rate is commonly associated with PFS and OS. Whole Exome sequencing of tumors from exceptional responders and non-responders is underway. A randomized phase 2-3 study of FOLFIRINOX vs. m FOLFIRINOX + CPI613 is scheduled to be initiated in late 2016.

Clinical trial identification: NCT01835041

Legal entity responsible for the study: Wake Forest University

Funding: Cornerstone pharmaceutical

Disclosure: All authors have declared no conflicts of interest.