ASCO GI 2022 #TPS632

Trial in Progress: Phase 1b Study of Vactosertib in Combination with nal-IRI plus 5FU/LV in Patients with Metastatic Pancreatic Ductal Adenocarcinoma who have Failed First-Line Gemcitabine/nab-Paclitaxel

Joon Oh Park, MD, PhD[1], Seung Tae Kim, MD, PhD[1], Jung Yong Hong, MD, PhD[1], Seong-Jin Kim, PhD[2], Young Suk Park, MD, PhD[1]

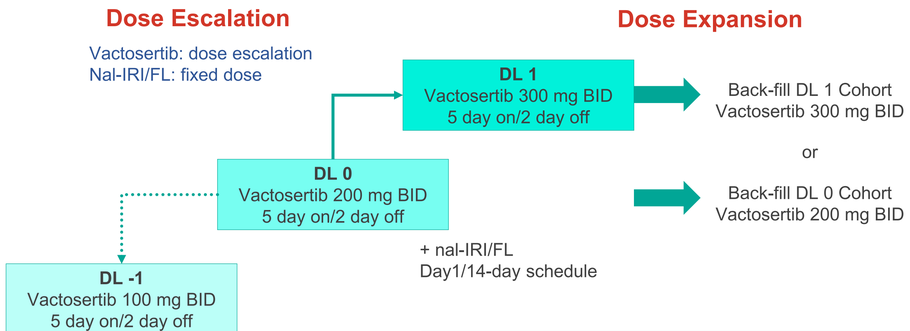
[1]Division of Hematology-Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [2]GILO Foundation, Seoul, Korea

INTRODUCTION

Background

- Pancreatic ductal adenocarcinoma (PDAC) remains one of the most aggressive malignancies and the leading cause of cancer-related death in the world, although recent advances in chemotherapies for metastatic PDAC provide better clinical outcomes.
- Liposomal irinotecan (nal-IRI) in combination with fluorouracil (5-FU) and folinic acid (LV), called the NAPOLI regimen, improves survival in advanced pancreatic cancer patients who failed gemcitabine-based chemotherapy.
- TGF-β is strongly involved in the tumor microenvironment of PDAC, and dysregulation of TGF-β signaling is a frequent molecular disturbance in PDAC progression and metastasis.
- Vactosertib is an orally bioavailable TGF-β signaling inhibitor that targets the TGF-β type I receptor kinase. In in vivo studies, vactosertib reduces cancer cell migration, invasion, and metastasis of various cancers, and combination of vactosertib with nal-IRI/5-FU/LV improves pancreatic cancer survival by suppressing cell migration, invasion, and epithelial-mesenchymal transition (EMT), highlighting a potential clinical application of this approach for PDAC patients (Hong et al, 2020).
- Based on this preclinical study, we develop a phase 1b study to determine the recommended phase 2 dose (RP2D) and to evaluate the safety of vactosertib in combination with nal-IRI/5FU/LV in patients with metastatic PDAC who have failed first-line gemcitabine/nab-paclitaxel.

STUDY DESIGN



Dose Escalation (3+3 design)

	Vactosertib	Nal-IRI /FL D1-14 q2wks
Dose level -1	**100 mg bid**	**100%**
Dose level 0	**200 mg bid**	**100%**
Dose level 1	**300 mg bid**	**100%**

STUDY OBJECTIVE

- **Primary**: To determine recommended phase 2 dose and to evaluate the safety of vactosertib in combination with nal-IRI/FL .
- **Secondary**
  - Progression-free survival (PFS)
  - Objective response rate (ORR)
  - Disease-control rate (DCR)
  - Overall survival (OS)
- **Exploratory:** PK, PD & biomarkers analysis

TREATMENT

- In the dose expansion part, one or two additional backfill cohorts among DL -1 through DL 1 will be opened for determination of the final RP2D. For each cohort, a maximum of 12 patients can be enrolled including the dose escalation and dose expansion phase.
- **Vactosertib** 100-300 mg orally twice per day 1-5 & day 8-12
- **NAPOLI regimen: nal-IRI + 5-FU/LV**
  - *Every 2weeks*
  - Nal-IRI 70 mg/m2 IV D1
  - Leucovorin 400 mg/m2 IV D1
  - 5-FU 2400 mg/m2 IV over 48hours D1, 2
- **Response evaluation**
  - *Every 6weeks*
  - Chest CT/A+P CT/Tumor marker/Blood sampling for translational research

STUDY INFORMATION

- **Status:** Recruiting
- **PI:** Joon Oh Park, M.D., Ph.D. (oncopark@skku.edu)
- **ClinicalTrial.gov Identifier:** NCT04258072

KEY ELIGIBILITY CRITERIA

Inclusion Criteria

- Histologically confirmed pancreatic adenocarcinoma
- Failed to gemcitabine-based chemotherapy for advanced pancreatic cancer
- Patients with measurable or evaluable lesion according to RECIST version 1.1
- Eastern Cooperative Oncology Group (ECOG) Performance status of 0 or 1
- Life expectancy of ≥ 12 weeks
- Adequate normal organ and marrow function measured within 7days prior to administration of study treatment
- Written informed consent

Exclusion Criteria

- Patients received other chemotherapy, including cytotoxic chemotherapy, immunotherapy, hormone therapy, within 14days prior to administration of IP
- Current or prior use of immunosuppressive medication
- Major surgical procedure within 28 days prior to the first dose
- Uncontrolled intercurrent illness, including ongoing or active infection
- History of another primary malignancy
- History of leptomeningeal carcinomatosis, brain metastasis or spinal cord compression

Reference

1. Hong E, et al, Sci Rep 2020 Feb 19: 19: 10:2935;
2. Wang-Gillam A, et al. Lancet. 2016 Feb 6;387(10018):545. ; Hoff PM, et al. J Clin Oncol. 2001 Apr 15;19(8):2282.
3. Siddiqui NS, et al. Expert Opin Pharmacother. 2019 Mar;20(4):399;
4. Yoo C et al. Ther Adv med Oncol 2019;11:1758835919871126.

Acknowledgement

Liposomal irinotecan is provided by by Servier and vactosertib is provided by MedPacto.