UC Irvine 趙 Chao Family Comprehensive Cancer Center

A Phase 1b Study of Gemcitabine (G) with Nab-paclitaxel with or without Pitavastatin (P) in the maintenance treatment of unresectable pancreatic adenocarcinoma (uPDAC)

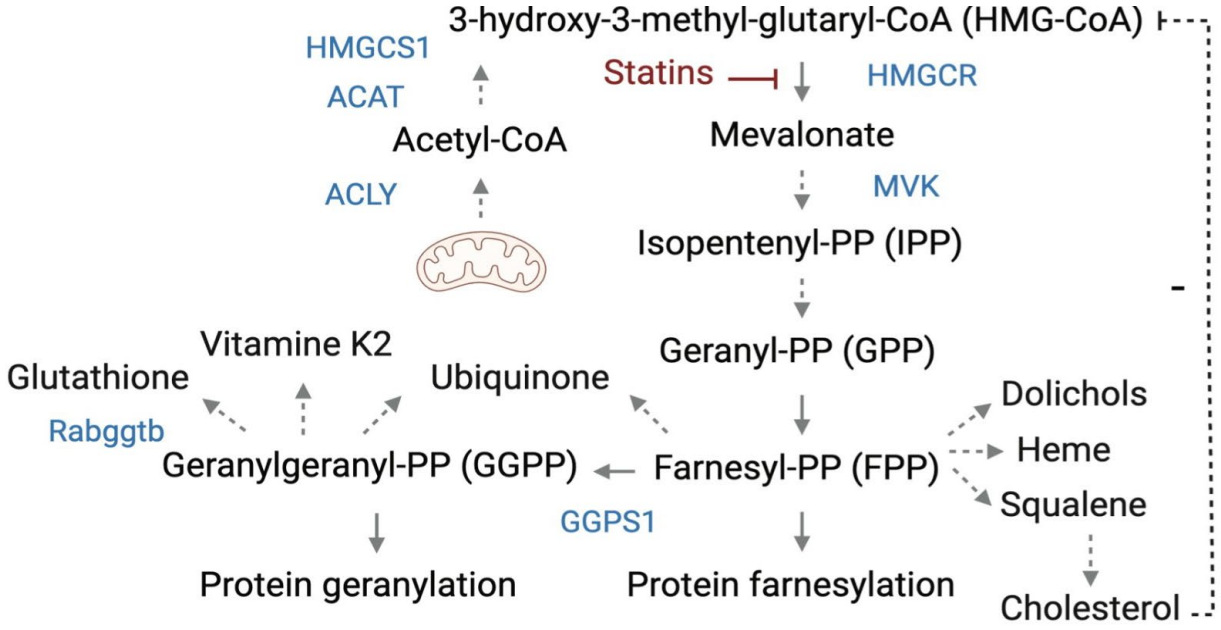
Jennifer Valerin, MD, PhD

2026 Scientific Retreat

November 5, 2026

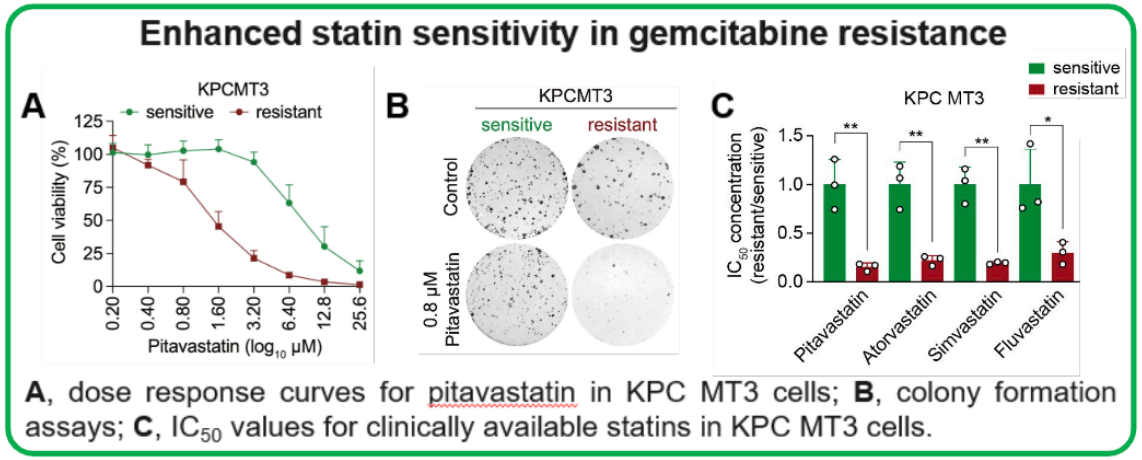
Resistance to Pancreatic Adenocarcinoma Treatment is Universal

- Pancreatic cancer remains one of deadliest cancers driven by lack of response and acquisition of chemoresistance
  - **5 year OS for metastatic disease: 3%**
- Current uPDAC SOC: **gemcitabine and nab-paclitaxel** combination shows synergy and safety over single agent chemo
- Targeting HMG-CoA reductase (rate limiting enzyme of mevalonate biosynthesis pathway) is actionable vulnerability in PDAC (Halbrook lab)

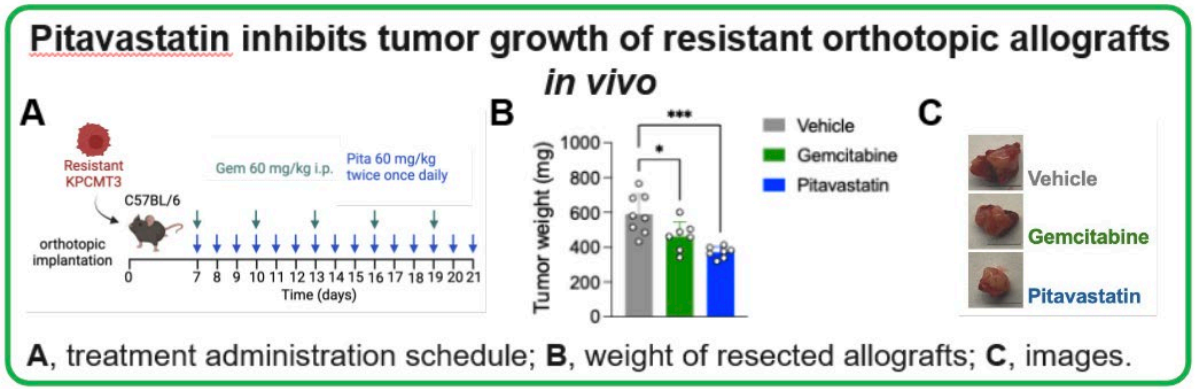


Pitavastatin has optimal pharmacokinetic properties to mediate anti-cancer therapy

- Statin studies show Pitavastatin has optimal pharmacokinetic properties to mediate anti-cancer therapy
- Gemcitabine and Pitavastatin Combination in Pre-clinical studies:
  - In vitro, synergistically suppressed proliferation of MIA PaCa-2 cells through sub-G1 and S phase cell cycle arrest, activation of apoptosis/necrosis, and activation of cellular metabolism
  - In vivo, inhibited tumor growth in Mia PaCa-2 xenografts



A, dose response curves for pitavastatin in KPC MT3 cells; **B**, colony formation assays; **C**, IC_{50} values for clinically available statins in KPC MT3 cells.



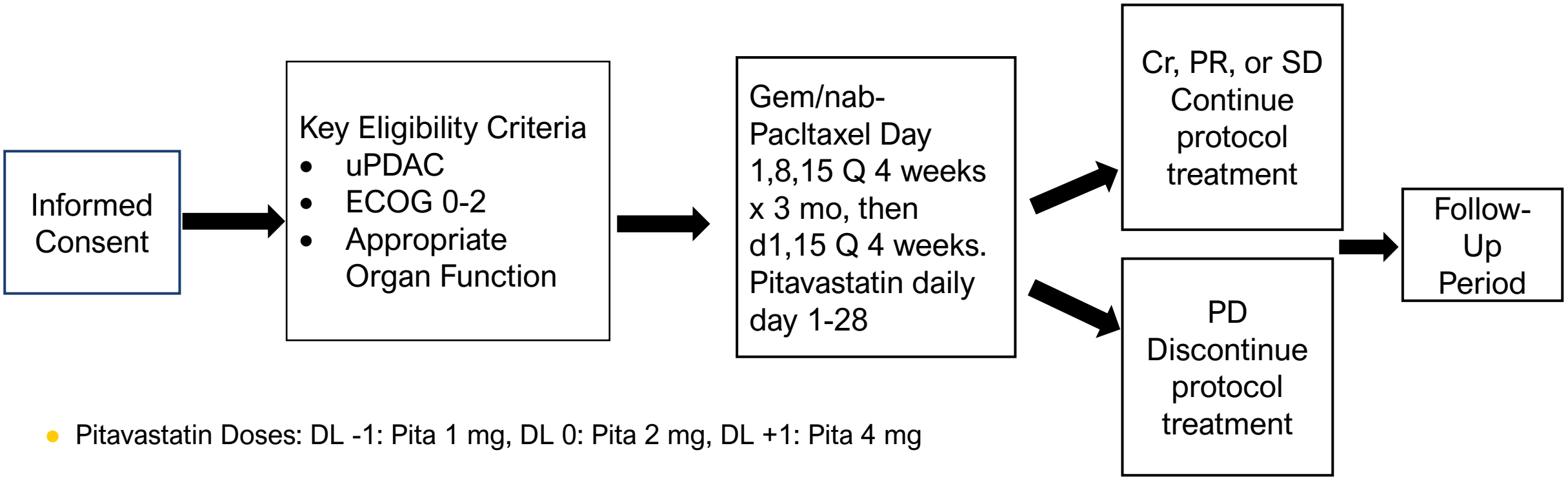
A, treatment administration schedule; **B**, weight of resected allografts; **C**, images.

- Influence of Diet on Pitavastatin Resistance: Pitavastatin's inhibitory activity in ovarian cancer in vitro and in mice xenografts was reversed by dietary geranylgeraniol requiring dietary changes

Michels et al Gastroenterology 2026

The Combination of Pitavastatin and Chemotherapy is Feasible and Tolerable

- **Hypothesis:** The combination of Pitavastatin (HMG-CoA reductase inhibitor) with Gemcitabine and nab-paclitaxel is feasible and tolerable and via sub-G1 and S phase cell cycle arrest, activation of apoptosis/necrosis and other crucial cytotoxic mechanisms, might improve outcomes in uPDAC.
- Trial Design: Single center, prospective, open label, non-randomized phase 1B trial (3+3 design)



- Pitavastatin Doses: DL -1: Pita 1 mg, DL 0: Pita 2 mg, DL +1: Pita 4 mg

Key Eligibility and Endpoints

- **Main Eligibility:**

Key Inclusion Criteria	Key Exclusion Criteria
a) 1L + uPDAC b) Age >=18 b) ECOG Performance Status 0-2 c) Life expectancy > 3 months d) Adequate organ function e) Ability to comply with treatment, pk and test schedules	a) Received other systemic therapy within 21 days of treatment b) another malignancy for which treatment is required c) clinically significant disease or co-morbidity d) symptomatic or progressing CNS metastases e) MI, arrhythmia, or symptomatic heart failure

- **Primary objective:**
  - Primary endpoint: RP2D of Pita in combination with Gemcitabine and nab-paclitaxel in treatment of uPDAC.
- **Secondary objectives:** PFS, OS, ORR (in patients with measurable disease)
- **Total number of pts to be enrolled:** *min= 8, max= 12 (includes anticipated screen failures)*

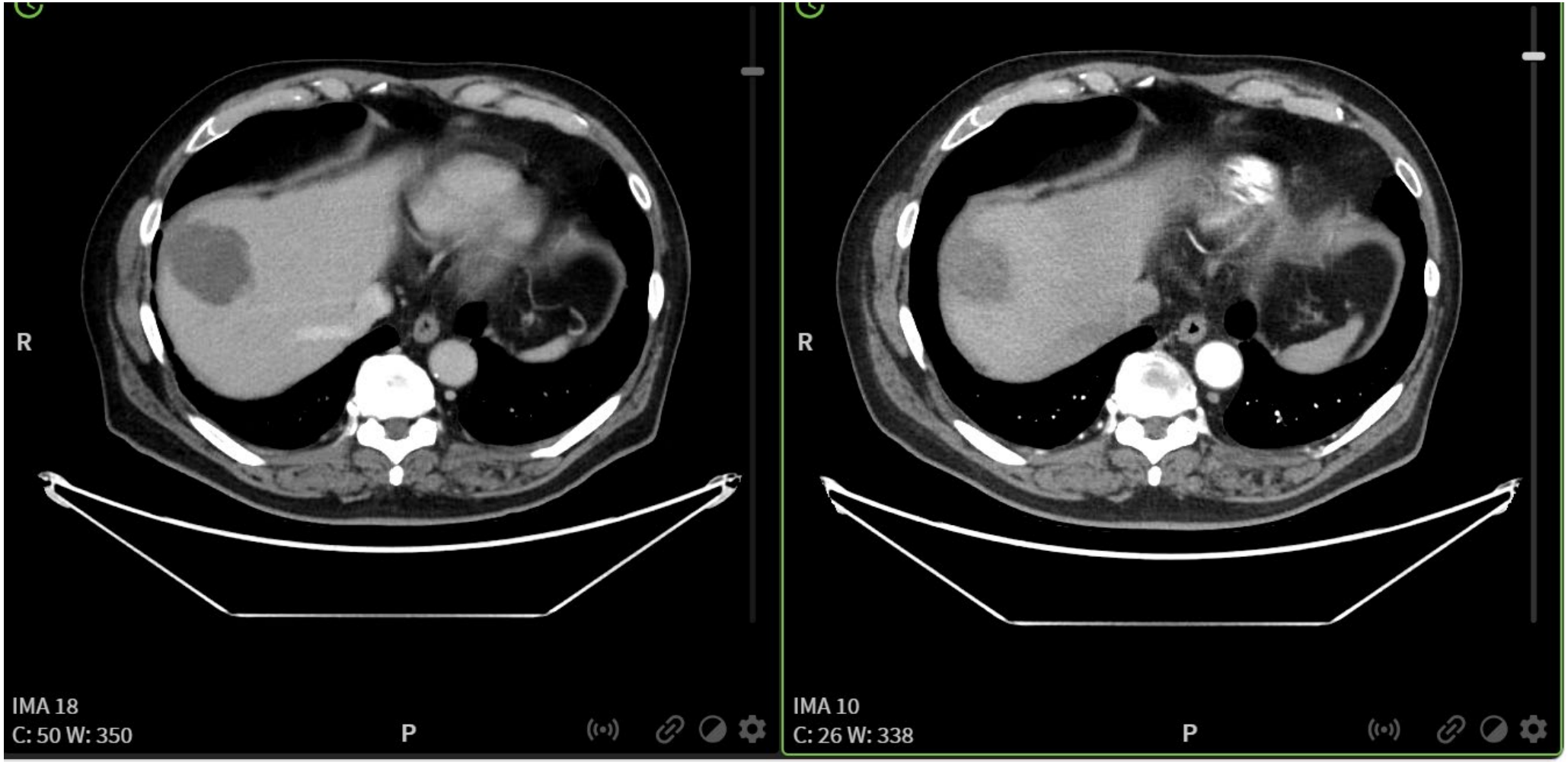
Preliminary Results Show Combination Therapy is Safe and Tolerable

- Two patients with metastatic PDAC have been enrolled to date on 2 mg Pitavastatin plus Chemo
- Patient 1: 68 yo F with metastatic PDAC originally diagnosed 12/13/24, treated with FOLFIRINOX and KRAS inhibitor (1/13/25-2/22/26)
  - Chemotherapy started 3/10/26, Study Treatment began 6/3/26
  - CA 19-9 declined from 377 → 17 (Nadir 7)
  - AE: Grade 1 flu-like symptoms, hematuria and vomiting
  - Best response: Stable Disease

- Patient 2: 74 yo M with metastatic PDAC originally diagnosed 8/27/24, treated with FOLFIRINOX and KRAS inhibitor (6/12/25-2/6/26)
  - Chemotherapy started 3/12/26, Study Treatment began 6/4/26
  - CA 19-9 declined from 38 → 10 (Nadir 7)
  - AE: Grade 1 leg edema and fever
  - Best response: Stable Disease

- No treatment related adverse events attributed to Pitavastatin
- Both patients remain on treatment exceeding the historical 5.1 mo PFS benchmark of 2L chemo
- Trial is currently on hold for protocol amendment and expected to reopen in about 1 month

CT Imaging Shows Marked Reduction in Size of Liver Lesion



5/21/26

9/22/26

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Thank you!

CFCCC Anti-Cancer Challenge

Halbrook laboratory (UC Irvine)

Colleagues: Farshid Dayyani, Zahra Hamedi, April Choi, Jason Zell, Fay-chi Lee, Misagh Karimi

Stern Center Staff (HPB team)

Patients