Intra-arterial Nanoparticle Therapy for Pancreatic Adenocarcinoma: Emerging Evidence and Therapeutic Potential

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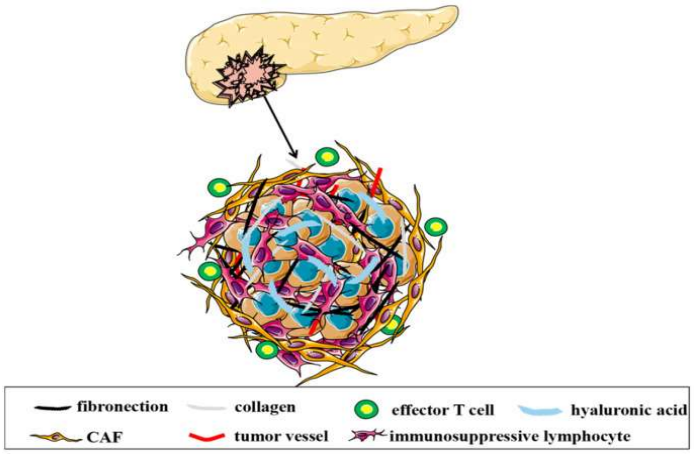
Background

- Pancreatic ductal adenocarcinoma (PDAC) has one of the poorest prognoses in oncology due to limited surgical options and a dense stroma that limits drug delivery.
- First-line treatment regimens uses the nanoparticle therapy IV nab-paclitaxel + gemcitabine, which offers modest survival benefits and remodeling of the tumor stroma (MPACT Phase III Trial, n=861).
- However, emerging evidence suggests that intra-arterial (IA) delivery of nanoparticle therapy may
  - Enhance targeted drug uptake
  - Reduce systemic toxicity
  - Potentially improve therapeutic response.



Hou W, Yang B, Zhu H. Nanoparticle-Based Therapeutic Strategies for Enhanced Pancreatic Ductal Adenocarcinoma Immunotherapy. Pharmaceutics. 2022 Sep 24;14(10):2033. doi: 10.3390/pharmaceutics14102033. PMID: 36297467; PMCID: PMC9607590.

Purpose

This educational exhibit reviews current clinical data on IA delivery of nanoparticle therapy in PDAC.

Materials and Methods

A review of clinical studies and ongoing clinical trials on IA nab-paclitaxel therapy was conducted using PubMed, focusing on the safety, efficacy, and clinical outcomes of this approach.

Results

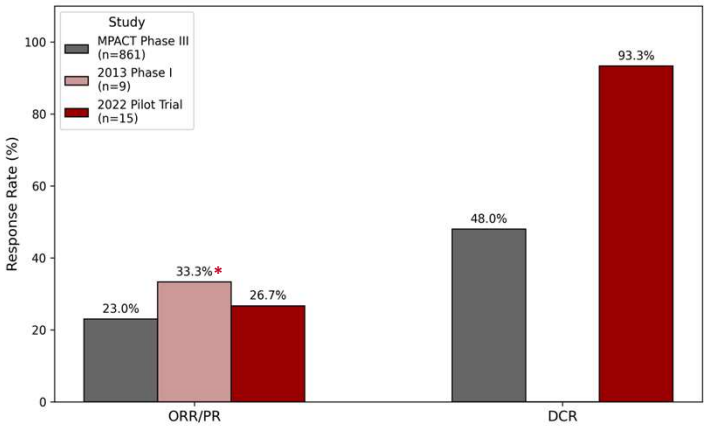
2013 Phase I Trial (hepatic IA nab-paclitaxel + IV gemcitabine/bevacizumab):

- Well tolerated
- PDAC subgroup (n=9): PR 33.3% vs 23% ORR in MPACT trial (IV nab-paclitaxel + gemcitabine, n=861)

2022 Pilot Clinic Trial (pancreatic IA nab-paclitaxel, n=15):

- Safe, rapid symptom relief
- ORR 26.7%, DCR 93.3% vs MPACT baseline (ORR 23%, DCR 48%)

Comparison of ORR/PR* and DCR across PDAC studies



ORR = Objective response rate. PR = Partial response rate. DCR = Disease control rate

Conclusions

- Early clinical data suggest that IA delivery of nanoparticle therapy may provide a therapeutic advantage in the treatment of PDAC.
- Compared to historical data on the current standard regimen of IV nab-paclitaxel/gemcitabine, IA nab-paclitaxel has demonstrated favorable response and disease control rates in small cohorts.
- While these findings are preliminary, they support further investigation of this approach through larger, comparative trials to better define the role of IA nanoparticle therapy in the treatment paradigm for PDAC.

References

1. Hou W, Yang B, Zhu H. Nanoparticle-Based Therapeutic Strategies for Enhanced Pancreatic Ductal Adenocarcinoma Immunotherapy. Pharmaceutics. 2022 Sep 24;14(10):2033. doi: 10.3390/pharmaceutics14102033. PMID: 36297467; PMCID: PMC9607590.
2. Von Hoff DD, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med. 2013 Oct 31;369(18):1691-703. doi: 10.1056/NEJMoa1304369. Epub 2013 Oct 16. PMID: 24131140; PMCID: PMC4631139.
3. Tsimberidou AM, Ye Y, Wheler J, Naing A, Hong D, Nwosu U, Hess KR, Wolff RA. A phase I study of hepatic arterial infusion of nab-paclitaxel in combination with intravenous gemcitabine and bevacizumab for patients with advanced cancers and predominant liver metastases. Cancer Chemother Pharmacol. 2013 Apr;71(4):955-63. doi: 10.1007/s00280-013-2088-y. Epub 2013 Feb 3. PMID: 23377373; PMCID: PMC3977741.
4. Wang N, Xu J, Wang G, Cao P, Ye X. Pancreatic intra-arterial infusion chemotherapy for the treatment of patients with advanced pancreatic carcinoma: A pilot study. J Cancer Res Ther. 2022 Dec;18(7):1945-1951. doi: 10.4103/jcrt.jcrt_819_22. PMID: 36647954.