Cancer Biol Med 2026. doi: 10.20892/j.issn.2095-3941.2025.0848

LETTER

Sequential nimotuzumab plus gemcitabine and nab-paclitaxel chemotherapy followed by irreversible electroporation in advanced pancreatic ductal adenocarcinoma: a retrospective real-world analysis

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Pancreatic ductal adenocarcinoma (PDAC) is among the deadliest solid tumors. Patients who develop PDAC with locally advanced pancreatic cancer (LAPC) or metastases have an especially poor prognosis[1]. Although there have been improvements in systemic therapy, long-term disease control is uncommon and most patients progress within months after treatment has started[2]. These issues underscore a critical, unmet need for rationally targeted multimodal approaches that enhance responses to systemic treatment and mitigate the long-standing chronic pathogenesis of local disease.

The most common drug regimen used in treating advanced PDAC is gemcitabine and nab-paclitaxel additives (AG)[3,4], which have conferred better outcomes in response and survival than gemcitabine alone but with temporary effects[5]. Consequently, efforts to improve cytoreduction gains during induction therapy are underway, such as use of the epidermal growth factor receptor (EGFR) pathway, which is overexpressed[6]. Nimotuzumab, a humanized anti-EGFR monoclonal antibody, has an excellent safety profile and demonstrates possible activity with chemotherapy based on gemcitabine in select PDAC patients and allowing sufficient disease control for an incremental phase of treatment[7].

Irreversible electroporation (IRE) is a non-thermal ablative modality that kills tumor cells by permanently proceeding to permeabilize the membranes without damaging collagenous frameworks, such as blood vessels and bile ducts[8]. The characteristics of IRE are desirable for pancreatic tumors with significant vascularity that are frequently inaccessible to surgical resection or ablation by heat[9]. Although IRE has been more actively integrated in the treatment of unresectable PDAC,

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Received January 13, 2026; accepted February 25, 2026; published online March 16, 2026.
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there are few real-world results relevant to the potential inclusion of IRE into a stepwise treatment paradigm in the wake of contemporary systemic therapies. Specifically, limited information that assesses the viability and preliminary success of a mix of nimotuzumab-based induction and consolidative IRE is available.

We attempted to bridge the gap in knowledge by performing a one-center retrospective real-world study on patients who underwent serial induction therapy with nimotuzumab plus AG, followed by consolidative IRE between January 2023 and December 2025. Patients were required to receive a minimum of three courses of induction therapy [nimotuzumab (200 mg/week), nab-paclitaxel (125 mg/m^2), and gemcitabine (1,000 mg/m^2) on days 1, 8, and 15 every 21 d], attain disease control (stable disease or partial response), according to RECIST version 1.1, and be in good working condition (Karnofsky Performance Status = 70). IRE was performed through open operation using an IRE therapeutic system (Tianjin Intelligent Health Medical Co., Ltd, China). Descriptive analysis was performed for procedural feasibility, adverse events associated with treatment rated using the Common Terminology Criteria for Adverse Events (version 4.0), radiographic response, and survival outcomes. This retrospective study protocol was reviewed and approved by the Ethics Committee of Tianjin Cancer Hospital Airport Hospital (Approval No. KY-2025-0295). The study adhered to the ethical standards outlined in Declaration of Helsinki.

The number of patients who underwent the entire sequential treatment pathway and became a part of the analysis was 26. An overview of the study design, patient selection, treatment sequence, and outcomes is shown in **Figure S1**. **Table S1** presents a summary of baseline demographic and clinical factors and shows that patients present with an overall stable performance status and balanced LAPC and limited liver-metastatic disease. The median age was 63 years, with male patients being the majority. There were 13 patients with LAPC, 13 patients with matched liver-metastatic PDAC and ≤3 synchronous hepatic lesions. **Figure 1A** depicts the patient screening and inclusion procedure, and **Figure 1B** shows the timelines of the separate treatments, i.e., induction therapy, IRE, and follow-up in the form of a swimmer plot.

Table S2 shows the radiographic and biochemical responses after induction therapy. The disease universal control was met and a 23.1% objective response rate was achieved; a stable state of the disease was observed in the remainder of the patients. The tumor size variation following induction therapy is represented in a waterfall plot (**Figure 1C**). A biochemical response, defined descriptively as a ≥50% reduction in serum carbohydrate antigen 19-9 (CA19-9), was noted in 61.5% of patients. **Table S3** summarizes adverse events related to treatment during induction therapy. Most events were low grade and containable; the electrolyte upsets, nausea, and vomiting were the most prevalent events. Hematologic or non-hematologic adverse events and treatment-related deaths were infrequent and were not higher than grade 3 at the time of induction. No grade 3 non-hematologic adverse events were reported.

All patients were manipulated to have a technologically successful form of consolidative IRE, which was 100% successful. **Table 1** lists the procedural characteristics and complications after IRE and shows local ablation to be a complication of the open pancreatic intervention. The most frequent complications were postoperative infections and pancreatic fistulas, which were managed in a conservative manner through conventional supportive care. One major vascular complication occurred that required intervention. It should be noted that there was no all-process mortality.

The median progression-free survival 15.2 months after the start of induction therapy was 7.2 months. The median local recurrence-free survival, computed from the date of IRE, was 7.3 months, indicating a sustained period of local disease stability at the primary pancreatic site following ablation. The overall survival had a median of 14.1 months (**Figure 1D-F**). Exploratory analyses, including descriptive subgroup comparison and Cox regression, were performed and should be interpreted as hypothesis-generating (**Figure S2**; **Tables S4 & S5**). A higher body mass index (BMI) and LAPC [*vs.* liver-metastatic pancreatic cancer (LMPC)] status were associated with longer progression-free and overall survival in exploratory multivariate models. **Figure S3** demonstrated longitudinal CA19-9 data through which the dynamics of heterogeneous biomarkers were observed in the IRE post-follow-up evaluation. Representative images of how the ablation zone normally progresses through initial changes of early peri-ablation to a non-enhancing stable scar can be seen in **Figure S4**.

Taken together, these data indicate that a multistate treatment approach comprised of nimotuzumab plus AG induction and consolidative IRE is clinically viable and could be safely applied to select patients with advanced PDAC. Successful local ablation was available to universality in case of induction therapy. Survival outcomes are descriptive and no comparative inference with other treatments is supported by the study design. Ideally, this method uses systemic therapy to reduce the amount of cells in the body and select the cells based on biological characteristics, then local consolidation is applied to manage the primary tumor, which in most cases widens morbidity and disease progression even in cases of metastatic disease[10].

This study evaluated a predefined clinical population consisting of patients who received induction therapy with nimotuzumab plus AG and subsequently underwent consolidative IRE according to multidisciplinary team (MDT) assessment. The retrospective, single-center design, small sample size, absence of a control group, and limited duration of follow-up (median 15.2 months) restrict broader generalization and assessment of long-term disease dynamics. Accordingly, the findings should be interpreted as descriptive and

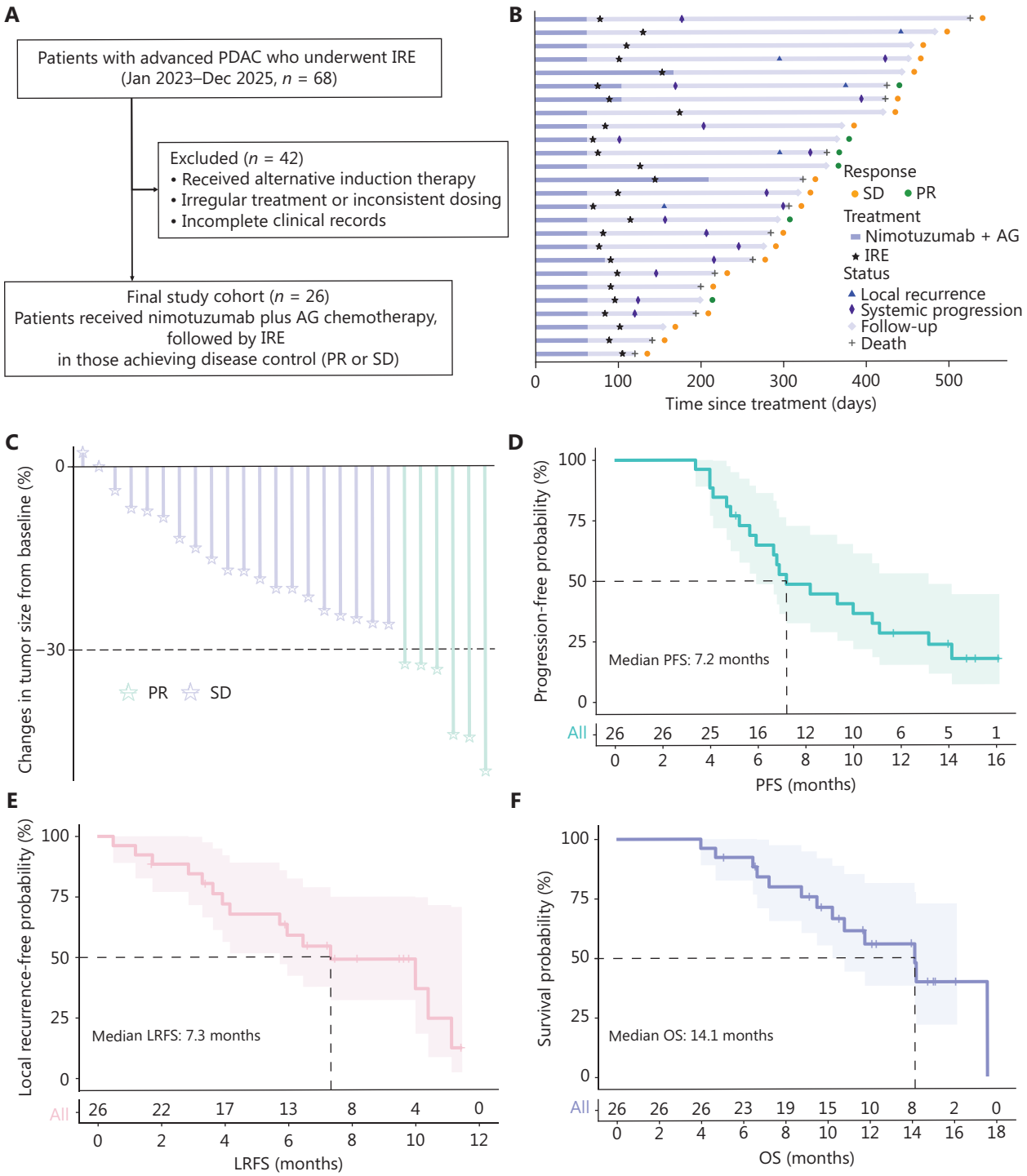


Figure 1 Study design and clinical outcomes. (A) Flowchart showing patient screening, eligibility assessment, and inclusion in the final analysis cohort. (B) Swimmer plot illustrates individual treatment timelines from the start of induction therapy through irreversible electroporation and subsequent follow-up. (C) Waterfall plot depicting the maximum percentage change from baseline in the sum of target lesion diameters after induction therapy, according to RECIST (version 1.1). (D–F) Kaplan–Meier curves showing (D) progression-free survival, (E) local recurrence-free survival from the date of IRE, and (F) overall survival. AG, gemcitabine plus nab-paclitaxel; IRE, irreversible electroporation; LRFS, local recurrence-free survival; OS, overall survival; PDAC, pancreatic ductal adenocarcinoma; PFS, progression-free survival; PR, partial response; SD, stable disease.

Table 1 IRE procedural characteristics and post-procedural outcomes (n = 26)

Procedural characteristics and outcomes	Value
Total operative time, median (range), min	120 (80–240)
Active ablation time, median (range), min	42.5 (6–140)
Number of electrodes, median (range)	4 (2–6)
Applied voltage range, V	1,800–3,000
Patients with concurrent liver ablation, *n* (%)	6 (23.1)
Post-IRE bleeding, *n* (%)	3 (11.5)
Post-IRE infection, *n* (%)	11 (42.3)
Pancreatic fistula, *n* (%)	6 (23.1)
Drainage tube placement, *n* (%)	10 (38.5)
Preoperative VAS score, median (range)	1 (0–2)
Postoperative VAS score, median (range)	1 (0–7)
Preoperative KPS score, median (range)	90 (90–100)
Postoperative KPS score, median (range)	90 (40–100)

IRE, irreversible electroporation; VAS, Visual Analog Scale; KPS, Karnofsky Performance Status.

hypothesis-generating observations specific to this predefined sequential treatment context, rather than evidence of comparative efficacy. However, the present research gives meaningful proof of the feasibility of combining efficient systemic therapy with non-thermal local ablation in severe PDAC. Future research is justified to narrow down the selection criteria of patients, treatment sequencing, and to explain the independent effect of local consolidation with IRE on survival and quality-of-life in such a challenging disease background.

Acknowledgments

The authors sincerely thank all patients whose medical records were included in this retrospective analysis.

Grant support

This study received support from Tianjin Health Science and Technology Project (Grant No. TJWJ2022MS007), the Science & Technology Development Fund of Tianjin Education Commission for Higher Education (Grant No. 2022ZD067), the Tianjin Municipal Science and Technology Bureau (Grant No. 22ZXJBSY00030), the National Key Laboratory of Druggability Evaluation and Systematic Translational Medicine (Grant No. 24ZXZSSS00440), and the Independent Project of the Key Laboratory of Drug Efficacy Evaluation and Systematic Translational Medicine, Tianjin Medical University Cancer Institute and Hospital (Grant No. QZ23-11).

Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

Conceived and designed the analysis: Jihui Hao, Chuntao Gao, Huikai Li.
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Contributed data or analysis tools: Yang Liu, Dandan Wu, Xing Li.
Performed the analysis: Yang Liu, Dandan Wu, Xing Li.
Wrote the paper: Yang Liu, Dandan Wu.
All authors reviewed and approved the final manuscript.

Data availability statement

The data generated in this study are available upon request from the corresponding authors.

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Cite this article as: Liu Y, Wu D, Li X, Zhang X, Li R, Ou Y, et al. Sequential nimotuzumab plus gemcitabine and nab-paclitaxel chemotherapy followed by irreversible electroporation in advanced pancreatic ductal adenocarcinoma: a retrospective real-world analysis. Cancer Biol Med. 2026; 23: 946-950. doi: 10.20892/j.issn.2095-3941.2025.0848