

Case Report



Profound Radiographic and Tumor-Lytic Response of Locally Advanced Pancreatic Adenocarcinoma to a Non-Systemic-Chemotherapy Multimodal Protocol—Fractionated Radiotherapy with Capecitabine Radiosensitization, Intratumoral EpCAM/CD3 Bispecific Antibody, Allogeneic NK and Autologous Lymphocyte Cellular Therapy, and Sequenced Pembrolizumab Following Failure of Conventional Gemcitabine-Based Therapy

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Abstract: Introduction: Locally advanced pancreatic adenocarcinoma (LAPC) carries a dismal prognosis with conventional therapy. Patients who progress on or plateau after first-line gemcitabine-based chemotherapy have limited evidence-based options outside of further cytotoxic regimens or palliative care. We report a case of profound radiographic and tumor-lytic response of bulky LAPC to a multimodal non-systemic chemotherapy protocol delivered after conventional standard of care had been exhausted. **Case:** A 56-year-old man originally diagnosed with pancreatic adenocarcinoma involving the bile duct in March 2023 received three cycles of gemcitabine at Mayo Clinic (Rochester, MN). His August 2024 PET/CT documented a partial response (pancreatic head SUV-max 3.0, down from 4.1). Over the subsequent 17 months, however, the disease progressed locoregionally. At admission to ICCA CancerCare (Hesieg Hospital, Tijuana, Mexico) on 26 January 2026, contrast CT documented a bulky pancreatic mass involving the bile duct measuring 101.3 mm × 93.68 mm. **Intervention:** The patient was treated 26 January–6 February 2026 with a multimodal protocol comprising (i) fractionated radiotherapy, 35 Gy in 10 sessions to the pancreatic tumor and adjacent lymph nodes; (ii) oral capecitabine 500 mg daily for 30 days as radiosensitization; (iii) two image-guided intratumoral injections of an EpCAM/CD3 bispecific T-cell-engaging antibody under ultrasound guidance and local anesthesia; (iv) four intravenous infusions of allogeneic natural-killer (NK) cells (100 million cells per infusion); (v) two intravenous infusions of autologous lymphocytes; (vi) two intravenous infusions of allogeneic mesenchymal stromal cells (MSCs, 50 million



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cells per infusion); (vii) two intravenous infusions of high-dose vitamin C; (viii) IV multivitamin/electrolyte support; (ix) IV esomeprazole 40 mg; and (x) anemia management with intravenous ferric carboxymaltose 500 mg twice and subcutaneous erythropoietin 2000 IU four times. The patient received no systemic cytotoxic chemotherapy at any point during ICCA care; capecitabine was administered at a sub-cytotoxic dose for radiosensitization only. Pembrolizumab (100 mg/4 mL) was administered on 18 March 2026, sequenced approximately six weeks after completion of the loading-phase EpCAM injections. A third intratumoral EpCAM injection was delivered on 15 April 2026. **Outcome:** Between completion of radiotherapy and administration of pembrolizumab, the tumor underwent clinically evident lysis, liquefying and draining through the patient's biliary catheter—a phenomenon consistent with the tumor-lytic effect of EpCAM/CD3 bispecific T-cell engagement that radiotherapy alone does not produce. Follow-up contrast CT on 13 May 2026 demonstrated a reduction in tumor dimensions to 87 mm × 72.9 mm with extensive necrotic areas within the residual mass—a substantial volumetric reduction with radiographic evidence of internal necrosis. Surveillance ¹⁸F-FDG PET/CT (14 May 2026) demonstrated only mild residual hypermetabolic activity in the pancreatic head, no bulky or hypermetabolic adenopathy, and no findings concerning metastasis. **Conclusions:** This case demonstrates that profound radiographic response, including clinically evident tumor lysis, can be achieved in bulky LAPC after failure of conventional gemcitabine chemotherapy using a multimodal protocol combining fractionated radiotherapy with capecitabine radiosensitization, intratumoral EpCAM/CD3 bispecific T-cell-engaging antibody, allogeneic NK and autologous lymphocyte cellular therapy, allogeneic MSC support, and sequenced pembrolizumab—without systemic cytotoxic chemotherapy and without surgical resection. The mechanistic framework (cancer-stem-cell-targeted T-cell engagement with cold-to-hot tumor microenvironment remodeling and cellular immune reinforcement) and the observed tumor-lytic clinical course warrant prospective evaluation in a registry cohort.

Keywords: locally advanced pancreatic adenocarcinoma; LAPC; pancreatic adenocarcinoma; bispecific antibody; EpCAM/CD3; intratumoral immunotherapy; allogeneic NK cells; autologous lymphocytes; mesenchymal stromal cells; capecitabine radiosensitization; pembrolizumab; tumor lysis; non-surgical management

1. Introduction

Pancreatic adenocarcinoma remains one of the most lethal solid tumors in modern oncology and is projected to become the second-leading cause of cancer-related mortality in the United States by 2030 [1]. Only approximately 15% of patients present with resectable disease at diagnosis [2], and even among those receiving conventional standard-of-care chemotherapy with gemcitabine—with or without nab-paclitaxel or FOLFIRINOX—median overall survival remains in the range of 10 to 24 months [3,4]. For locally advanced pancreatic adenocarcinoma (LAPC), defined by major arterial encasement or extensive venous involvement [5], the standard treatment paradigm of palliative chemotherapy with or without radiotherapy delivers durable disease control in only a minority of patients [6,7].

Recent investigations have explored the combination of stereotactic body radiotherapy (SBRT), cytotoxic chemotherapy, and immune checkpoint inhibitors as a strategy to convert unresectable disease toward resectability and to extend survival [8,9]. McCarthy and colleagues described near-complete pathological response in a patient with LAPC treated with SBRT and a PD-1 inhibitor followed by surgical resection [10], and Bi and colleagues recently reported a successful non-surgical case of LAPC managed with a switch from first-line gemcitabine and S1 (G&S) chemotherapy to albumin-bound paclitaxel, capecitabine, and the PD-1 inhibitor camrelizumab, achieving complete remission at 45 months despite KRAS and TP53 mutations [11]. These reports, however, all retain systemic cytotoxic chemotherapy as a backbone of the post-failure regimen.

Here we report the case of a 56-year-old man with bulky LAPC following a plateau of response to first-line gemcitabine, treated at ICCA CancerCare with a multimodal protocol that, in this patient, used no standard-dose systemic cytotoxic chemotherapy. The regimen combined fractionated radiotherapy with sub-cytotoxic-dose

capecitabine radiosensitization, two image-guided intratumoral injections of an EpCAM/CD3 bispecific T-cell-engaging antibody, allogeneic natural-killer cell and autologous lymphocyte cellular therapy, allogeneic mesenchymal stromal cell support, and sequenced pembrolizumab. The clinical course included a striking tumor-lytic event between completion of radiotherapy and administration of the checkpoint inhibitor, with the tumor liquefying and draining through the patient's biliary catheter—a phenomenon consistent with the mechanism of intratumoral T-cell-engager-driven tumor-cell killing that radiotherapy alone does not produce. To our knowledge, this is the first published case of profound radiographic and tumor-lytic response in bulky LAPC achieved with an intratumoral EpCAM/CD3 bispecific T-cell-engaging antibody delivered without concurrent systemic cytotoxic chemotherapy.

2. Case Presentation

A 56-year-old white man was originally diagnosed in March 2023 with pancreatic adenocarcinoma involving the bile duct. Endoscopic ultrasound-guided fine-needle aspiration at Mayo Clinic in May 2024 (case NR-24-9013) returned a diagnosis of adenocarcinoma; immunohistochemistry was positive for EpCAM, AE1/AE3, CK7, and CDX-2 (focal), and negative for CD31, chromogranin, ERG, inhibin, GLUT-1, synaptophysin, INSM1, and trypsin. SMAD4 demonstrated patchy immunoreactivity. Past surgical history was notable for cholecystectomy and biliary drain/stent placement. The patient presented at ECOG performance status 1.

2.1. Auxiliary Examinations at Initial Workup

Baseline laboratory values obtained at Mayo Clinic on 28 August 2024 (during the course of first-line chemotherapy) showed normocytic anemia (hemoglobin 10.0 g/dL, hematocrit 30.7%), preserved leukocyte and platelet counts, monocytosis ($1.06 \times 10^9/L$), and a lymphocyte count of $1.11 \times 10^9/L$. Glucose was 114 mg/dL with hemoglobin A1c 6.6%, consistent with pancreatogenic (type 3c) diabetes. Hepatic and renal function were preserved (AST 21 U/L, ALT 31 U/L, alkaline phosphatase 125 U/L, total bilirubin 0.5 mg/dL, creatinine 1.07 mg/dL, eGFR 82 mL/min/BSA). Prothrombin time was mildly prolonged (14.0 s; INR 1.3) without therapeutic anticoagulation. The serum carcinoembryonic antigen (CEA) level was 10.5 ng/mL (reference ≤ 3.0 ng/mL).

2.2. Initial Conventional Treatment (Mayo Clinic, 2024)

Under the direction of medical and surgical oncology at Mayo Clinic, the patient received three cycles of single-agent gemcitabine. He was not taken to operative resection. ^{18}F -FDG PET/CT performed 29 August 2024 documented partial metabolic response: pancreatic head focal SUV-max in the area of clear malignancy decreased from 4.1 (23 May 2024) to 3.0, while overall pancreatic head SUV-max of 5.9 was attributed in part to peri-stent inflammation. No findings concerning for metastasis were identified at that time. The reading radiologist explicitly characterized the study as partial response.

2.3. Interval Progression and Referral to ICCA CancerCare

Over the subsequent 17 months, the patient did not undergo surgical resection. He was referred to ICCA CancerCare for integrative oncology evaluation. At admission (Hesieg Hospital, Tijuana, Baja California, Mexico) on 26 January 2026, contrast CT of the abdomen and pelvis (RV Intervencionista, Tijuana) demonstrated a bulky pancreatic adenocarcinoma involving the bile duct measuring 101.3 mm $\times$ 93.68 mm in maximal axial dimensions, consistent with locoregional disease progression relative to the prior partial-response state. Surgical clips from prior cholecystectomy were noted, and a biliary stent/catheter remained in place. There was no imaging-defined evidence of distant metastatic disease at admission.

2.4. Treatment at ICCA CancerCare (26 January–6 February 2026)

Following a multidisciplinary review at ICCA, the patient was enrolled in a multimodal integrative oncology protocol delivered fully outpatient at Hesieg Hospital and affiliated COFEPRIS-authorized facilities in Tijuana, BC. The patient received no systemic cytotoxic chemotherapy during ICCA care. The components administered during the loading phase (26 January–6 February 2026) are summarized in Table 1 and detailed below.

- (i) Fractionated radiotherapy. Fractionated external-beam radiotherapy delivering 35 Gy in 10 sessions to the pancreatic tumor and adjacent lymph nodes, initiated on 26 January 2026.
- (ii) Capecitabine radiosensitization. Oral capecitabine 500 mg once daily for 30 days, administered at a sub-cytotoxic dose as a radiosensitizing agent only. The patient did not receive systemic cytotoxic chemotherapy at standard doses at any point during ICCA care.

- (iii) Intratumoral EpCAM/CD3 bispecific antibody. Two sequential image-guided intratumoral injections of a proprietary EpCAM/CD3 bispecific T-cell-engaging antibody, manufactured on behalf of ICCA CancerCare in GMP-approved laboratories, were administered into the pancreatic tumor under ultrasound guidance and local anesthesia during the loading phase. A third intratumoral injection was subsequently administered on 15 April 2026. The intratumoral route of administration, concentrating polyclonal T-cell activation at the tumor site while limiting systemic on-target off-tumor exposure in EpCAM-expressing normal epithelia, is a defining feature of this protocol and the principal point of differentiation from systemically administered T-cell-engaging therapeutics. The antibody was administered at a concentration of 24 µg in a volume of 1 mL. The release criteria was: (a) sterility: no growth; (b) endotoxin: ≤5 EU/kg per maximum administered dose; and (c) purity: ≥95% HPLC, with aggregates ≤5%.
- (iv) Allogeneic natural-killer cell therapy. Four intravenous infusions of allogeneic NK cells, 100 million cells per infusion, were administered during the loading phase.
- (v) Autologous lymphocyte therapy. Two intravenous infusions of autologous peripheral blood lymphocytes, collected by simple venous blood draw rather than leukapheresis.
- (vi) Allogeneic mesenchymal stromal cell therapy. Two intravenous infusions of allogeneic fresh umbilical cord-derived (Wharton's jelly) mesenchymal stromal cells, 50 million cells per infusion, were administered. The product was prepared at the ICCA CancerCare COFEPRIS-authorized GMP cell and tissue laboratory; release criteria included passage 3 to 4 at infusion, viability greater than 90% by trypan blue exclusion, and surface marker characterization meeting International Society for Cellular Therapy (ISCT) minimum criteria for MSC identity (CD73⁺, CD90⁺, CD105⁺, and CD34⁻/CD45⁻/HLA-DR⁻).
- (vii) Adjunctive support. Two intravenous infusions of high-dose vitamin C; IV multivitamin and electrolyte support; and IV esomeprazole 40 mg.
- (viii) Anemia management. The patient had baseline normocytic anemia from prior chemotherapy, expected to be exacerbated by upper-abdominal radiotherapy. Anemia was managed with intravenous ferric carboxymaltose (Renegy) 500 mg twice, and subcutaneous erythropoietin 2,000 IU on four occasions. In our clinical experience, anemia management is frequently required during radiotherapy directed at the liver, pancreas, or rectum, and maintenance of adequate erythrocyte mass is mechanistically important to tumor oxygenation and radiosensitivity.
- (ix) Sequenced checkpoint inhibition. Pembrolizumab 100 mg/4 mL was administered intravenously on 18 March 2026, sequenced approximately six weeks after completion of the loading-phase EpCAM intratumoral injections.

The mechanistic rationale of the intratumoral EpCAM/CD3 bispecific antibody is the bridging of the EpCAM antigen—broadly expressed on pancreatic adenocarcinoma cells, including the cancer stem cell compartment implicated in recurrence—to CD3 on cytotoxic T-lymphocytes, resulting in polyclonal T-cell activation and perforin/granzyme-mediated tumor-cell apoptosis independent of MHC restriction [12]. When delivered intratumorally, this mechanism achieves locally concentrated T-cell activation. Subsequent damage-associated molecular pattern (DAMP) release, CXCL9/CXCL10-mediated recruitment of natural-killer cells and dendritic cells, and lymph-node trafficking of tumor antigens by activated dendritic cells underlie the conversion of the historically immunologically cold pancreatic tumor microenvironment toward a hot, immune-responsive state [13–16]. The intravenous allogeneic NK cell, autologous lymphocyte, and MSC infusions reinforce the cellular immune compartment systemically.

Table 1. Timeline of clinical course. EUS-FNA, endoscopic ultrasound-guided fine-needle aspiration; SUV-max, maximum standardized uptake value; PET/CT, positron emission tomography–computed tomography; RT, radiotherapy; MSC, mesenchymal stromal cell; IV, intravenous; PO, per os.

Date	Event	Details
March 2023	Initial diagnosis	Pancreatic adenocarcinoma involving the bile duct
May 2024	EUS-FNA confirmation	Mayo Clinic case NR-24-9013: adenocarcinoma confirmed; IHC profile characterized
May–Aug 2024	Conventional chemotherapy	Three cycles of single-agent gemcitabine at Mayo Clinic; no surgical resection

Table 1. Cont.

Date	Event	Details
29 Aug 2024	PET/CT (Mayo)	Partial response; pancreatic head focal SUV-max 3.0 (from 4.1); no metastasis
Sept 2024–Jan 2026	Interval progression	Locoregional progression 16 months without further systemic therapy at the index institution
26 Jan 2026	ICCA baseline CT	Bulky pancreatic mass involving the bile duct: 101.3 mm × 93.68 mm
26 Jan–6 Feb 2026	Multimodal loading phase	Radiotherapy 35 Gy in 10 fractions; capecitabine 500 mg PO daily × 30 d (radiosensitization); 2× intratumoral EpCAM/CD3 bispecific antibody; 4× allogeneic NK cell IV (100M each); 2× autologous lymphocyte IV; 2× MSC IV (50M each); 2× IV vitamin C; IV multivitamins; IV esomeprazole; ferric carboxymaltose 500 mg × 2 and erythropoietin 2000 IU × 4 for anemia
Feb–Mar 2026	Tumor-lytic event	Between RT completion and pembrolizumab: tumor liquefied and drained via biliary catheter—consistent with intratumoral T-cell-engager-driven cytotoxicity
18 Mar 2026	Pembrolizumab	Sequenced anti-PD-1 checkpoint inhibition, 100 mg/4 mL IV
15 Apr 2026	3rd intratumoral injection	Additional EpCAM/CD3 bispecific antibody injection
13 May 2026	Surveillance CT	Tumor reduced to 87 mm × 72.9 mm with extensive internal necrosis
14 May 2026	Surveillance PET/CT	Only mild residual hypermetabolic activity in the pancreatic head; no nodal involvement; no metastasis

2.5. Tumor-Lytic Event and Imaging Response

Between completion of radiotherapy and administration of pembrolizumab, the patient experienced a clinically evident tumor-lytic event: the pancreatic tumor liquefied and drained through the indwelling biliary catheter. This phenomenon may be mechanistically consistent with the cytotoxic effect of intratumoral EpCAM/CD3-bispecific-antibody-driven polyclonal T-cell activation, and is not a finding produced by external-beam radiotherapy alone at the doses delivered (35 Gy in 10 fractions).

Follow-up contrast CT on 13 May 2026 demonstrated reduction in tumor dimensions to 87 mm × 72.9 mm (from the 101.3 mm × 93.68 mm pre-treatment baseline) with extensive necrotic areas within the residual mass. By the cross-product approximation of axial dimensions, this represents an approximately 33% reduction in measured cross-sectional area, accompanied by radiographic evidence of internal tumor necrosis—a response pattern consistent with effective intratumoral immunotherapy rather than simple radiotherapy-mediated cytoreduction.

Surveillance ¹⁸F-FDG PET/CT performed 14 May 2026 demonstrated stable appearance of the pancreatic head with atrophy and only mild hypermetabolic activity. There were no bulky or hypermetabolic lymph nodes, no hypermetabolic lesions in the head/neck or chest, and no concerning osseous findings. The combined CT and PET/CT interpretation—substantial dimensional reduction with internal necrosis on contrast CT, and absent bulky hypermetabolic disease and no metastasis on PET/CT—supports a profound clinical response (Figure 1: Pre- and Post-Treatment Abdominal CT Imaging; Figure 2: Surveillance PET/CT—Absence of Metastatic Disease.).

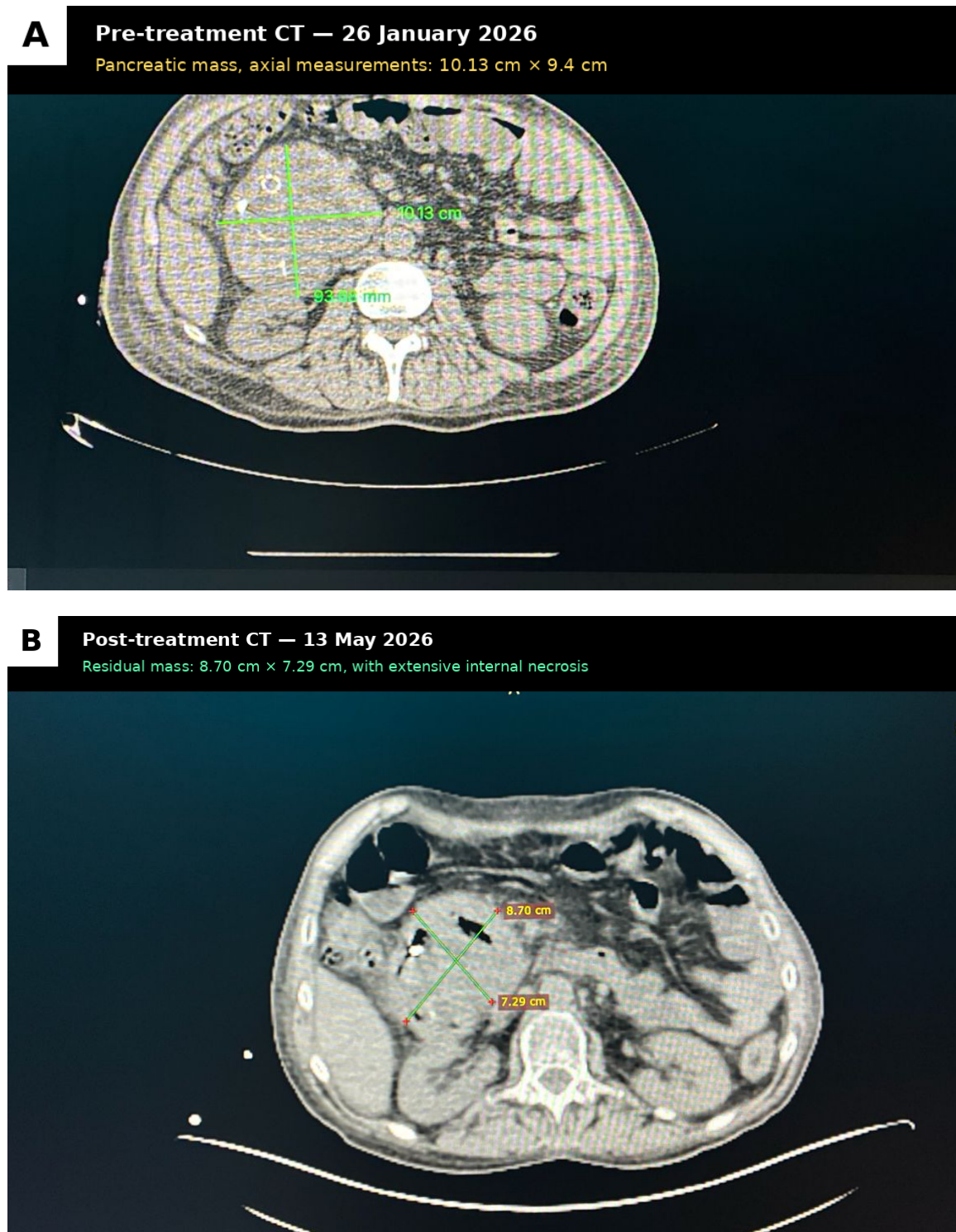


Figure 1. Axial contrast CT images of the pancreatic mass before and after the ICCA multimodal protocol. **(A)** Pre-treatment study (26 January 2026, RV Intervencionista, Tijuana) demonstrating a bulky pancreatic mass involving the bile duct, measuring 10.13 cm × 9.4 cm (101.3 mm × 93.68 mm) in maximal axial dimensions. **(B)** Post-treatment study (13 May 2026, Sidney Health Center) demonstrating reduction in maximal axial dimensions to 8.70 cm × 7.29 cm, with extensive internal necrotic transformation visible within the residual mass. Cross-product area reduction approximately 33%. Patient identifiers have been redacted to preserve confidentiality.

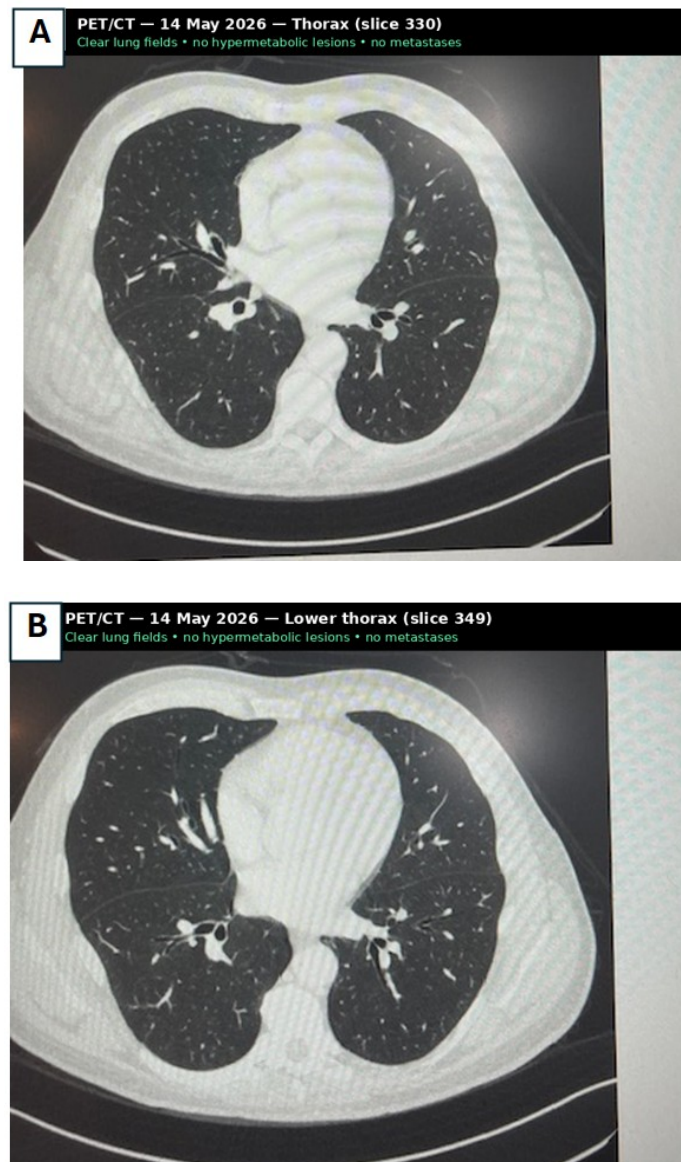


Figure 2. Representative axial slices from the surveillance ^{18}F -FDG PET/CT performed 14 May 2026. (A) Upper thoracic slice (image 330 of 1108) and (B) lower thoracic slice (image 349 of 1108) demonstrate clear lung fields without hypermetabolic lesions. The complete study documented no bulky or hypermetabolic adenopathy, no hypermetabolic lesions in the head/neck or chest, and no findings concerning for distant metastatic disease.

2.6. Post-Loading Continuation

Following the loading phase, the patient received pembrolizumab 100 mg/4 mL on 18 March 2026 and a third intratumoral EpCAM/CD3 bispecific antibody injection on 15 April 2026. The patient remained clinically stable at follow-up, with maintained ECOG performance status and outpatient functional capacity. Continued surveillance is planned at three-month intervals (CBC, comprehensive metabolic panel, hemoglobin A1c, prothrombin time/INR, and CEA), with cross-sectional imaging at six-month intervals.

3. Outcome

The clinical course of this patient included two distinct response signals. The first was the clinically evident tumor-lytic event between completion of radiotherapy and administration of pembrolizumab, in which the pancreatic tumor liquefied and drained through the indwelling biliary catheter. The dose and schedule of radiotherapy delivered (35 Gy in 10 fractions) is not, in our clinical experience, sufficient to produce this magnitude of tumor lysis in isolation; the temporal correlation with the intratumoral EpCAM/CD3 bispecific antibody injections, and the absence of any other agent in the regimen with comparable cytotoxic potential at the doses given, supports the interpretation that the immunologic component of the multimodal protocol was the proximate cause of the lysis.

The second response signal was the radiographic response on follow-up imaging: tumor dimensions decreased from 101.3 mm × 93.68 mm at ICCA baseline to 87 mm × 72.9 mm on 13 May 2026 contrast CT, with extensive internal necrosis. By the cross-product approximation, the measured cross-sectional area decreased by approximately 33%, and the residual mass exhibited radiographic features of internal necrotic transformation—a pattern consistent with effective intratumoral immunotherapy rather than simple radiotherapy-mediated cytoreduction. Surveillance ¹⁸F-FDG PET/CT one day later confirmed only mild residual hypermetabolic activity in the pancreatic head, with no bulky adenopathy and no metastatic disease.

Performance status, glycemic control, and biliary drainage have remained stable on the post-loading continuation regimen. Tumor marker surveillance (CEA, baseline 10.5 ng/mL at Mayo) and serial cross-sectional imaging are ongoing on quarterly and semiannual schedules, respectively.

4. Discussion

The case we describe is, to our knowledge, the first published account of profound radiographic response and clinically evident tumor lysis in bulky locally advanced pancreatic adenocarcinoma achieved with an intratumoral EpCAM/CD3 bispecific T-cell-engaging antibody delivered without concurrent systemic cytotoxic chemotherapy and without surgical resection. This distinguishes the present case from the recent literature on non-surgical management of LAPC, which has uniformly retained a cytotoxic chemotherapy backbone alongside checkpoint-inhibitor immunotherapy [10,11].

Bi and colleagues recently reported complete remission in a 60-year-old woman with KRAS- and TP53-mutant LAPC who, after failure of first-line gemcitabine/oxaliplatin/S-1 chemotherapy, was switched to albumin-bound paclitaxel, capecitabine, and the PD-1 inhibitor camrelizumab [11]. That regimen—although successfully avoiding surgical resection—depended on a continued cytotoxic chemotherapy backbone in combination with a systemic checkpoint inhibitor. Similarly, McCarthy and colleagues described near-complete pathological response with SBRT plus pembrolizumab followed by surgical resection [10]. The present case extends the non-surgical paradigm one step further: the operative immunotherapeutic mechanism is intratumorally delivered, antigen-targeted, T-cell-engaging, and the systemic cytotoxic chemotherapy component familiar to those prior reports is absent. The clinically evident tumor-lytic event observed in our patient provides direct mechanistic support for this interpretation.

We believe addition of allogeneic NK cells improved efficacy of the radiation therapy, as well as of the intratumoral bispecific antibody. It is known that radiation induces expression of numerous stress induced ligands which activate NK cells.

The study illustrates the potential synergy obtained when combining mechanistically divergent immunomodulatory approaches. For example, EpCAM is highly expressed on pancreatic adenocarcinoma cells, with particularly relevant expression on the cancer stem cell (CSC) population implicated in chemoresistance and recurrence. CD3 T cells are directed to attack EpCAM expressing cells since the CD3-bispecific T-cell engagers redirect endogenous polyclonal T-cells, driving perforin/granzyme-mediated apoptosis independent of MHC restriction [12]. When delivered intratumorally rather than systemically, this mechanism achieves locally concentrated T-cell activation while limiting on-target off-tumor toxicity in EpCAM-expressing normal epithelia. Subsequent DAMP release, CXCL9/CXCL10-mediated recruitment of NK cells and dendritic cells, and lymph-node trafficking of tumor antigens by activated dendritic cells underlie the conversion of the historically immunologically cold pancreatic tumor microenvironment toward a hot, immune-responsive state [13–16]. The intravenous allogeneic NK cell and autologous lymphocyte infusions delivered in parallel reinforce the cytotoxic effector compartment systemically.

Capecitabine at 500 mg PO daily—substantially below standard cytotoxic dosing—was administered as a radiosensitizing agent only, consistent with the well-established role of fluoropyrimidine radiosensitization in gastrointestinal radiotherapy. We emphasize that capecitabine at this dose and schedule does not function as systemic cytotoxic chemotherapy in the conventional sense; the role here is exclusively to enhance the radiotherapeutic effect locally. Anemia management with intravenous ferric carboxymaltose and subcutaneous erythropoietin was undertaken because radiotherapy to the pancreas characteristically exacerbates anemia, and adequate erythrocyte mass is mechanistically important to tumor oxygenation and radiosensitivity. We have observed in our practice that anemia management is frequently required during radiotherapy directed at the liver, pancreas, or rectum, and consider it a meaningful adjunct to multimodal protocols of this type.

Several caveats apply. First, this is a single-patient observation, and the response described, while profound, does not constitute proof of cure; long-term follow-up beyond the six-month post-treatment time point is needed. Second, the post-treatment study of 13 May 2026 (contrast CT) and the surveillance study of 14 May 2026 (FDG

PET/CT with non-contrast attenuation-correction CT) provide complementary but distinct information; together they support a profound response, but the modality difference precludes formal RECIST-based measurement-to-measurement comparison with the original baseline. Third, although the patient received no systemic cytotoxic chemotherapy during ICCA care, the interval between gemcitabine completion in 2024 and ICCA admission in 2026 means a delayed or carryover effect of prior chemotherapy on the immune microenvironment cannot be formally excluded. Fourth, molecular tumor characterization (KRAS, TP53, PD-L1, MSI/MMR status) was not obtained for this patient. These markers were neither available from prior care nor requested by the ICCA clinical team, as systemic cytotoxic chemotherapy was not part of the planned regimen and these markers, while relevant to chemotherapy and systemic checkpoint inhibitor response in pancreatic cancer [11,17–20], are not currently used to guide the components of the ICCA protocol delivered. We acknowledge this as a limitation for cross-study comparison and recommend that prospective registry data incorporate molecular characterization to enable subgroup analysis.

Despite these caveats, the case is, in our view, important. This study suggests that in patients with LAPC who have plateaued or progressed on conventional gemcitabine-based therapy, a multimodal protocol combining fractionated radiotherapy with capecitabine radiosensitization, intratumoral CSC-targeted bispecific T-cell engagement, allogeneic NK and autologous lymphocyte cellular therapy, and sequenced checkpoint inhibition can deliver profound radiographic response with clinically evident tumor lysis without systemic cytotoxic chemotherapy and without surgical resection. The framework is hypothesis-generating and warrants prospective evaluation in a registry cohort.

5. Literature Review

A targeted literature review of non-surgical and post-chemotherapy salvage strategies for LAPC was conducted using PubMed, Scopus, and Web of Science. Four exemplar reports of patients with pancreatic cancer achieving favorable outcomes with immunotherapy-incorporating regimens after standard-of-care failure are summarized below.

Comparing the present case to those summarized in Table 2, three distinctive features emerge. First, the index patient achieved a profound radiographic response and clinically evident tumor lysis without any standard systemic cytotoxic chemotherapy delivered during the multimodal ICCA protocol, whereas all four comparator cases in the published literature retained a cytotoxic chemotherapy backbone or interventional cytoreductive procedure alongside immunotherapy. Second, the immunotherapeutic mechanism is delivered intratumorally and is antigen-targeted (EpCAM/CD3) rather than relying on systemic immune-checkpoint blockade alone, and is supported by parallel intravenous allogeneic NK and autologous lymphocyte infusions to reinforce the cytotoxic effector compartment systemically. Third, the protocol explicitly targets the cancer stem cell compartment via EpCAM, addressing a recognized driver of pancreatic cancer recurrence [21,22].

Table 2. Selected published cases of non-surgical or post-failure immunotherapy-based management of pancreatic adenocarcinoma. LAPC, locally advanced pancreatic adenocarcinoma; PDAC, pancreatic ductal adenocarcinoma; PACC, pancreatic acinar cell carcinoma; SBRT, stereotactic body radiotherapy; TACE, transarterial chemoembolization; TMB, tumor mutational burden; Ab, antibody.

Author	Age	Sex	Diagnosis	Intervention	Outcome
McCarthy et al., 2021 [10]	83	F	LAPC (PDAC)	SBRT + pembrolizumab + surgical resection	Near-complete pathologic response; no recurrence
Bi et al., 2025 [11]	60	F	LAPC, KRAS/TP53 mut, PD-L1 28%	Nab-paclitaxel + capecitabine + camrelizumab (PD-1)	Complete remission at 45 months; no surgery
Zhu et al., 2023 [19]	49	F	Pancreatic head ca. + liver metastases	TACE (gem/cis) + microwave ablation + immunotherapy	Satisfactory therapeutic response

Table 2. Cont.

Author	Age	Sex	Diagnosis	Intervention	Outcome
Xu et al., 2021 [20]	68	M	PACC, PD-L1+, high TMB	Gem/nab-paclitaxel + SOX + toripalimab (PD-1)	Satisfactory response; good tolerance
Schramm et al. (present)	56	M	Bulky LAPC post-gemcitabine plateau (101.3 × 93.68 mm)	RT 35 Gy/10fx + capecitabine radiosensitization + intratumoral EpCAM/CD3 bispecific Ab + allo NK + auto lymphocytes + MSCs + pembrolizumab (no systemic chemo)	Tumor lysis with biliary drainage; 33% area reduction; internal necrosis; no metastasis

6. Conclusions

We report a case of bulky locally advanced pancreatic adenocarcinoma in which a multimodal protocol of fractionated radiotherapy with capecitabine radiosensitization, three intratumoral injections of an EpCAM/CD3 bispecific T-cell-engaging antibody, allogeneic natural-killer cell and autologous lymphocyte cellular therapy, allogeneic mesenchymal stromal cell support, and sequenced pembrolizumab—delivered without standard-dose systemic cytotoxic chemotherapy and without surgical resection—produced clinically evident tumor lysis and profound radiographic response after first-line gemcitabine chemotherapy had plateaued. The mechanistic framework (cancer-stem-cell-targeted intratumoral T-cell engagement with cellular immune reinforcement and cold-to-hot tumor microenvironment remodeling) and the observed clinical course support a prospective registry evaluation. We propose that intratumoral antigen-targeted bispecific T-cell engagement, combined with focal radiation, cellular immune reinforcement, and sequenced checkpoint inhibition, represents a non-cytotoxic-chemotherapy paradigm for LAPC patients in whom conventional therapy has been exhausted.

Author Contributions

H.S.: Conceptualization, Clinical Direction, Methodology, Writing—original draft, Writing—review & editing. R.R.: Clinical Care, Data curation, Validation, Writing—review & editing. A.M.: Clinical Care, Investigation, Validation, Writing—review & editing. Y.M.: Clinical Operations, Methodology, Project administration, Writing—review & editing. S.S.: Clinical Care, Investigation, Writing—review & editing. T.I.: Scientific consultation, mechanistic interpretation, Writing—review & editing. G.D.: Conceptualization, Project administration, Resources, Supervision, Writing—original draft, Writing—review & editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

All clinical care described herein was delivered at Hesieg Hospital and affiliated facilities operating under authorization of the Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS), Tijuana, Baja California, Mexico. The patient provided written informed consent for inclusion of clinical, imaging, and treatment data in this case report and for publication of de-identified imaging. The protocol components are delivered under physician-directed clinical administration in accordance with ICCA CancerCare's COFEPRIS-authorized framework.

Informed Consent Statement

Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this article. A copy of the consent form is on file with the corresponding author and is available for review by the journal upon request.

Data Availability Statement

The de-identified clinical, laboratory, and imaging data supporting the findings of this case report are available from the corresponding author upon reasonable request, subject to applicable privacy regulations.

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Conflicts of Interest

HS serves as Chief Medical Officer of ICCA CancerCare. YM serves as Chief Operating Officer of ICCA CancerCare. GD serves as Founder and Chief Executive Officer of ICCA Inc., DBA ICCA CancerCare, and ACOR Inc. RR, AM, SS, and TI report no conflicts of interest beyond their roles as listed.

Use of AI and AI-Assisted Technologies

The authors used a generative artificial intelligence assistant (Anthropic Claude) to assist with manuscript drafting, structuring, and language editing. The clinical data, treatment decisions, patient assessment, imaging interpretation, and scientific claims presented herein originate entirely from the treating clinicians and authors. All AI-assisted text was reviewed, verified, and edited by the authors, who take full responsibility for the content, accuracy, and integrity of the manuscript.

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