Narrative Review
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The Possible Role of Immunotherapy in Locally Advanced Pancreatic Cancer Treatment*

Rouan Barakat[1, 2], Despoina Sidira[1, 2], Athanasios Stavropoulos[1], Nikias Konsolas[1], Andreas Palantzas[1], Dimitrios Filippou[1, 2]

[1]Department of Anatomy, Medical School of Athens, National and Kapodistrian University of Athens, Greece, [2]Research and Education Institute in Biomedical Sciences, Piraeus, Greece

Correspondence: *r1barakat@hotmail.com*; Tel.: +30 695 5119216

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Abstract

Objective. Locally advanced pancreatic cancer (LAPC) represents a significant subset of pancreatic cancers and is characterized by a poor prognosis and limited treatment options. Conventional therapies, including chemoradiotherapy, have demonstrated limited success, prompting interest in innovative strategies, such as immunotherapy. This review evaluates the role of immunotherapy in LAPC. **Materials and Methods.** For this review, a comprehensive search of the PubMed database was conducted in August 2024. After applying the exclusion criteria, 26 studies were included in the analysis. **Results.** Immune checkpoint inhibitors have produced inconsistent clinical outcomes, with modest improvements in progression-free survival and significant side effects. Cancer vaccines, particularly GVAX in combination regimens, have demonstrated potential, as have fibroblast activation protein (FAP) and mKRAS-specific amphiphile vaccines in preclinical and clinical settings. Chimeric antigen receptor (CAR) T-cell therapies targeting various antigens have yielded encouraging outcomes but have faced safety and efficacy challenges. Emerging approaches, including Toll-like receptor agonists, tumor-associated macrophage targeting, and radioimmunotherapy, have also shown preclinical promise but require further study. Despite numerous investigations, the overall impact of immunotherapy on LAPC remains limited. Some combination therapies involving checkpoint inhibitors, vaccines, and CAR T cells have shown positive outcomes; however, many are hindered by the immunosuppressive environment and toxicity of tumors. Recent studies emphasize the need for further research to refine these strategies and improve treatment options. **Conclusion.** LAPC remains one of the deadliest malignancies, with immunotherapy offering potential but constrained by limited survival benefits and adverse effects. Further studies focusing on novel agents, refined combinations, and overcoming tumor resistance mechanisms are critical to improve outcomes for this challenging disease.

Key Words: Locally Advanced Pancreatic Cancer ▪ Immunotherapy ▪ Oncology ▪ Immune Checkpoint Inhibitors.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is a malignancy associated with a dismal prognosis and is currently the seventh most prevalent cause of cancer-related mortality globally (1). A significant proportion of pancreatic adenocarcinomas are deemed non-resectable upon diagnosis due to the presence of locally advanced or metastatic disease. The five-year survival rate for individuals diagnosed with PDAC is below 5% (2), while locally advanced pancreatic cancer (LAPC)—characterized by a tumor that has yet to disseminate to distant sites but is invasive within and surrounding the pancreas, obstructing major blood vessels—constitutes one-third of all pancreatic cancer diagnoses. In cases of locally advanced disease, the efficacy of chemoradiotherapy is increasingly scrutinized. This underscores the urgent need for the development of innovative strategies, novel

*The present work is attributed to the Department of Anatomy, Medical School of Athens, National and Kapodistrian University of Athens, Greece.

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pharmacological agents, and additional research in this field. Notably, literature references from 1998 and 2002 have already advocated for the incorporation of immunotherapy in the treatment of pancreatic cancer (3, 4).

This review aimed to evaluate the potential role of immunotherapy in the management of LAPC.

Materials and Methods

This review aimed to evaluate the impact of immunotherapy on LAPC. To achieve this objective, a comprehensive search was undertaken in August 2024 on the PubMed database utilizing the search term "the role of immunotherapy in locally advanced pancreatic cancer". The search yielded a total of 55 articles published between 1991 and 2024. To focus exclusively on the most relevant and constructive details, specific exclusion criteria were applied during the evaluation of the articles. The criteria were as follows: articles must relate to LAPC; studies should discuss immunotherapy options either in experimental or current clinical contexts; and the articles must present statistically significant results. Additionally, the selected articles were required to be written in English, available in full text to maintain uniformity, and accessible in full text through the PubMed database. Following the application of these criteria, 29 articles were excluded, leaving a total of 26 articles that were included in this review.

Results

Firstly, clinical trials assessing immune checkpoint inhibitors for LAPC have shown inconsistent results. Agents targeting programmed cell death protein ligand-1 (PD-L1) and programmed cell death protein 1 (PD-1), such as pembrolizumab, nivolumab, durvalumab, and spartalizumab, were explored in early-phase studies (1, 2, 5-11). Some trials indicated a slight enhancement in progression-free survival, while most reported limited success, averaging 4-5 months for median progression-free survival (1, 6, 7, 10, 11). Additionally, some researchers have noted an increase in cluster of differentiation 8+ (CD8+) T-cell infiltration in the tumor microenvironment in several patients, although the sample sizes were too small for a statistical review (9). Treatments involving anti-cytotoxic T-lymphocyte associated protein-4 (anti-CTLA-4) agents, such as ipilimumab and tremelimumab, have produced similar results, showing no significant objective responses in the majority of studies (6, 10).

Regarding vaccines: cancer vaccine research has focused on peptide-based, whole-cell, and neoantigen-targeted strategies. Peptide vaccines (e.g., GV1001 and mesothelin) have largely failed to deliver meaningful clinical benefits (2). In contrast, the GVAX vaccine appeared promising in early-phase trials, improving disease-free survival when used in conjunction with therapies such as CRS-207 or PD-1 inhibitors such as nivolumab (8, 12). A neoantigen-targeted vaccine utilizing hyaluronic acid gel (PancVax) exhibited T-cell stimulation and decreased recurrence in preclinical settings, while an mKRAS-specific vaccine triggered a notable T-cell response in almost half of the participants in a clinical trial, albeit accompanied by mild side effects (6).

Moreover, CAR T-cell therapies targeting mesothelin, CD133, and human epidermal growth factor receptor-2 (HER-2) antigens have shown promising results but have encountered safety and efficacy issues. While preclinical evaluations of anti-mesothelin CAR T-cells indicated tumor shrinkage, clinical studies demonstrated stable disease in only a small proportion of patients (13, 14). Treatment targeting CD133 achieved partial remission in 28.57% of subjects but was linked to adverse effects, such as leukopenia and nausea (14). HER-2 CAR T-cell studies had limited efficacy, revealing isolated cases of stable disease alongside significant adverse reactions, including severe toxicity (12, 14).

We now examine the combinations of the aforementioned therapies. Combination regimens that integrate checkpoint inhibitors, cancer vaccines, and standard treatments have resulted in mixed outcomes. For example, the combination of GVAX and ipilimumab resulted in improved survival

rates compared to individual therapies, while stem cell inhibition with chemotherapy (gemcitabine/nab-paclitaxel) yielded a 35% objective response rate (2). Notably, intratumoral Toll-like receptor-7 agonists combined with PD-1 blockade have shown enhanced therapeutic benefits in preclinical studies, highlighting the potential of multifaceted treatment approaches (5).

Furthermore, adoptive T-cell therapies featuring cytokine-induced killer (CIK) cells have shown safety profiles but limited effectiveness, achieving a median period of stable disease lasting 11 weeks (8). Likewise, natural killer (NK) cell-based therapies have shown dose-responsive effects but no substantial survival advantage (5). Other experimental strategies, such as radioimmunotherapy targeting CD-147 and beta-7-homolog-3 protein (B7-H3), have yielded encouraging preclinical findings but require further examination (1).

Finally, initial trials targeting tumor-associated macrophages, myeloid suppressor cells, and innovative immune targets have shown promise in boosting immune responses and enhancing clinical outcomes. For example, vaccination using mucin-1 (MUC-1) pulsed dendritic cells allowed for long-term survival in one-third of patients observed for four years (15).

Discussion

To better understand the mechanisms underlying pancreatic cancer, several key immune-related factors influence disease progression and therapeutic response. $CD8^+$ T cells, also known as cytotoxic T lymphocytes, play a critical role as they can directly eliminate cancer cells, and their presence is generally associated with an improved prognosis. However, the tumor microenvironment often counteracts this benefit through mechanisms such as regulatory T cells (Tregs), which suppress anti-tumor immune responses, and KRAS mutations, which foster an immunosuppressive milieu that impairs effective immunity. Conversely, tumors with deficient mismatch repair or microsatellite instability (MSI) display a high tumor mutation burden (TMB) and generate abundant neoantigens, rendering them more immunogenic and more likely to respond to immunotherapy. Emerging therapeutic strategies, such as bispecific antibodies, aim to overcome these barriers. For example, CEA-TCB, which redirects $CD3^+$ T cells toward CEA-expressing pancreatic tumor cells in a manner similar to bispecific T-cell engagers (BiTEs), has shown encouraging results in preclinical pancreatic ductal adenocarcinoma (PDAC) models. It not only enhanced $CD8^+$ T-cell infiltration and reduced tumor burden but also demonstrated synergy with PD-L1 blockade, highlighting its potential to transform the typically immune-cold pancreatic tumor microenvironment into one more amenable to immune-mediated clearance (12).

In the current study, we assessed papers that employed different kinds of possible immunotherapy options for LAPC treatment. The therapies evaluated were immune checkpoint inhibitors, vaccines, CAR T-cell therapies, NK cell / other T-cell therapies, and combination therapies of the above. The results of each study are analyzed below.

Immune Checkpoint Inhibitors

The articles under review predominantly examined the utilization of immune checkpoint inhibitors as a promising therapeutic strategy for immunotherapy in LAPC. Numerous studies have emphasized the application of anti-PD-L1 and anti-PD-1 agents as potential treatment modalities for this specific type of cancer (1, 2, 5-11, 16). In particular, pembrolizumab, nivolumab, durvalumab, and, in one instance, spartalizumab, were primarily administered during phase I or II clinical trials, as detailed in the analyzed studies (11, 17). Despite the variety of these immune checkpoint inhibitors, the results have been largely unsatisfactory, characterized by brief progression-free survival rates (ranging from 4 to 5 months), attributed to factors such as limited immunogenicity and an immunosuppressive tumor microenvironment associated with pancreatic cancer (1, 7, 10, 11, 16). Moreover, although an increase in CD8(+) T-cells was noted within the tumor microenvironment, the sample size of the patient cohort was too small to attain

statistical significance, encompassing only 2 patients (9). The remaining investigations concerning PD-L1 and PD-1 inhibitors indicated more promising outcomes, exemplified by a disease control rate of 100% and a median progression-free survival of 7.9 months, particularly benefiting patients exhibiting a deficient mismatch repair phenotype or microsatellite instability (MSH-I), who demonstrated an increased overall response rate (2, 16). These findings are supported by the KEYNOTE-158 Phase II trial (NCT02628067), which demonstrated that while dMMR or MSI-H tumors are generally more immunogenic and responsive to PD-1 blockade due to their high mutational burden, pancreatic cancer shows limited responses, reflecting its highly immunosuppressive tumor microenvironment. Other studies have yielded similar results, including a response rate of 18.2%, a progression-free survival period of 2.1 months, an overall survival time of 4 months, and heightened radiosensitivity observed in PDAC tumors (5, 6). Additionally, several studies have assessed anti-CTL4 therapies, specifically ipilimumab and tremelimumab, in phase II trials (2, 9, 10, 16). Unfortunately, the majority of these studies reported a lack of objective responses (10, 16). Conversely, other studies have reported tumor reductions at the preclinical level, a decrease in carbohydrate antigen 19-9 (CA19-9) serum levels, or an enhancement in median progression-free survival by 7.9 months, along with a 100% disease control rate (2, 9). Furthermore, inhibitors targeting C-C chemokine receptor type 2 (CCR2), CC chemokine receptor (CCR), C-X-C chemokine receptor (CXCR), and colony-stimulating factor 1 receptor (CSF1R) have been similarly examined (4, 16). The use of CCR2 inhibitors alone resulted in an objective response rate of 49%, whereas their combination with CSF1R inhibitors significantly increased T-cell infiltration within the tumor microenvironment in an animal model (4, 16). In addition, the combination of CCR inhibitors with C-X-C chemokine receptor-2 (CXCR2) inhibitors produced an overall enhancement in the therapeutic response. CD 40 agonists administered alongside gemcitabine or complement C2 inhibitors were also investigated as promising treatment avenues. Unfortunately, these agents did not have a significant impact on LAPC (9, 10). Finally, indoleamine 2,3-dioxygenase (IDO) inhibitors, such as indoximod, achieved a 37% objective response rate when used in conjunction with gemcitabine and nab-paclitaxel (16).

Vaccines

This study investigated the role of cancer vaccines in the treatment of LAPC. Initially, various studies focused on peptide-based cancer vaccines featuring antigens such as mesothelin or MUC1, designed to activate autologous dendritic cells alongside telomerase phase III vaccination (GV1001) or vaccinations targeting the Wilms' tumor protein-1 (WT1) antigen in combination with gemcitabine. Unfortunately, these investigations did not yield any notable clinical benefits (2). Another significant category of vaccines examined was whole cell cancer vaccines, with GVAX being a prominent example; it is a tumor cell vaccine incorporated with the granulocyte-macrophage colony-stimulating factor (GM-CSF) gene. GVAX was utilized either as a monotherapy or in conjunction with other therapeutic agents (12). Notably, GVAX alone demonstrated enhanced disease-free survival in phase I and II clinical trials (12). When combined with cyclophosphamide administered one day prior to GVAX or with the CRS-207 vaccine, a recombinant Listeria-based cancer vaccine containing a live-attenuated strain expressing human mesothelin, a two-month improvement was observed in phase II trials. However, these results were not statistically significant in phase III trials (2, 8, 13). Furthermore, a phase II trial assessed the combination of GVAX/CRS-207 with nivolumab (anti-PD-1) or ipilimumab (a CTLA-4 inhibitor), revealing promising outcomes only when paired with nivolumab (8, 12). Subsequent investigations have uncovered additional vaccines, such as the FAP vaccine, which appears to inhibit tumor progression, enhance the efficacy of immune checkpoint inhibitors, and provoke both spontaneous and vaccine-induced immune responses (18).

Furthermore, research involving a neoantigen-targeted vaccine administered via a hyaluronic acid hydrogel (PancVax gel) demonstrated a decrease in local recurrence following incomplete tumor resection and elicited T-cell activation in response to PancVax (19). Conversely, disappointing results have been reported in studies focusing on Algenpantucel-L, which is composed of irradiated cancer cells expressing alpha-1,3-galactosyltransferase coupled with radiochemotherapy in postoperative scenarios (2). Lastly, a phase I clinical trial in 2024 evaluated an mKRAS-specific amphiphile vaccine on 25 patients harboring KRAS mutations, yielding encouraging results; 21 of the 25 patients exhibited therapeutic responses, with 52% reaching a T-cell response above the median (100% biomarker reduction and 46% tumor clearance). Nonetheless, adverse effects such as fatigue, injection site reactions, and myalgia were also noted (20).

CAR T-Cell Therapies

Among the various adoptive T-cell transfer therapies, CAR T-cell therapy is the most promising option (2). CAR T-cells are genetically engineered T-cells programmed to recognize specific tumor-associated antigens via their chimeric receptors (13). Recent studies have highlighted two antigens, anti-mesothelin and carcinoembryonic antigen, as being particularly effective for T-cell activation (2). Moreover, the efficacy of these targeted therapies is significantly augmented when they are administered in conjunction with other immune modulators, such as cyclophosphamide or anti-CTLA4 and anti-PD1 agents (2). Preclinical trials involving anti-mesothelin CARs in murine models have demonstrated prolonged survival and reduced tumor burden (14). However, in a clinical trial (NCT01897415), only one out of six patients displayed disease progression (N=1/6; 17%), while two patients achieved stable disease for durations of 3.8 to 5.4 months (N=2/6; 33.4%), and the clinical outcomes for the remaining three patients remained indeterminate (N=3/6; 50%) (13, 14). Notably, no adverse events (AEs) were observed during this clinical trial (14). In another phase I clinical trial (NCT02159716) involving lentiviral-transduced anti-mesothelin (anti-MSLN) CAR T-cells (either combined with or without cyclophosphamide), 11 out of 15 patients experienced short-term stable disease (14). Common AEs, such as nausea and mild fatigue, have also been reported (14). However, it is essential to recognize that numerous clinical trials are still in their early phases (14). Overall, CAR T-cells targeting mesothelin showed acceptable tolerance, but their efficacy remains limited (12).

Other studies have identified alternative targets for CAR T-cells. CD133, which is significantly expressed in pancreatic ductal adenocarcinoma (PDAC), is a potential target (14). In a phase I clinical trial (NCT02541370), where all participants exhibited over 50% CD133 expression, 2 out of 7 patients (28.57%) experienced partial remission, while 3 out of 7 (42.85%) achieved stable disease, with the remaining 2 (28.57%) showing disease progression (14). Post-treatment evaluations indicated that CD133-positive cells were no longer detected in the tumor biopsies (14). Additionally, serious side effects reported included leukopenia, thrombocytopenia, anemia, anorexia, nausea, and mucosal hyperemia (14). Moreover, trials utilizing epidermal growth factor receptor (EGFR) targeted CAR T-cells were specifically conducted for metastatic PDAC, which lies outside the scope of this review (14).

In addition, over 60% of patients with PDAC show HER-2 overexpression, suggesting the potential for HER-2-targeted CAR T-cells (13). In a phase I clinical trial (NCT01935843), two patients achieved stable disease lasting 5.3 and 8.3 months (14). However, previous studies have indicated that anti-HER-2 CAR T-cell treatment could lead to severe AEs (grades 2 and 3) and even fatalities within 15 min of infusion (14).

In summary, the use of CAR T-cells for LAPC presents several safety concerns (15). Finally, it should be highlighted that allogeneic CAR T-cell infusions may also incur life-threatening AEs (14).

Natural Killer Cells/Other T-Cells

In addition to CAR T-cells, another type of T-cell immunotherapy has been tested. Cytokine-induced killer cells (CIK), which are ex vivo expanded, were evaluated in a phase II study, which showed encouraging outcomes (8). Although 3 patients (15%; N=20) reported grade 3 AEs such as weakness and thrombocytopenia, this trial suggests a relatively safe therapy with uncertain efficacy, as the median period of stable disease was reported as 11 weeks, and quality-of-life measures appeared to improve (8).

Chimeric antigen receptor natural killer cells (CAR NK-cells) have also been recognized in the literature, although reliable clinical outcomes are lacking (14). However, CAR NK-cells used in other conditions have resulted in serious grade 3 and 4 AEs (14). Further studies have reported that KPC (Kras, p53, and Cre) cells genetically engineered to express the carcinoembryonic antigen (CEA) were implanted into CEA transgenic mice. When the tumors reached sizes of 100-300 mm^3, the mice received either vehicle control injections or immunotherapy treatments (CEA-transcutaneous bilirubinometers [TCB] and/or aPD-L1). Treatment with CEA-TCB, either alone or in conjunction with aPD-L1, inhibited tumor growth, whereas aPD-L1 alone had no significant impact. Additionally, therapies involving CEA-TCB appeared to be linked to an increase in CD8 T-cell numbers, which were inversely correlated with tumor size (21).

Combination Therapies

This section focuses on treatment regimens that incorporate multiple therapeutic modalities. Current studies are testing the combination of mesenchymal stem cells with various immunotherapies, although these investigations are still in their early stages (1). Moreover, ongoing phase II studies are exploring the synergy between Ulocuplumab and Nivolumab (2). The combination of GVAX with ipilimumab has shown promising outcomes, particularly concerning survival rates, compared with ipilimumab alone (2). Additionally, a large trial is examining stem cell inhibition in combination with gemcitabine/nab-paclitaxel (2). The results are summarized in Table 1.

The table presents an overview of studies evaluating combinations of immunotherapies, chemotherapies, targeted agents, radiotherapy, and cellular therapies. The reported outcomes encompass survival statistics, tumor reduction, objective response rates, and immune response indicators, and clarify whether the results stem from clinical trials or preclinical studies, alongside pertinent limitations (such as adverse effects, trial terminations, or insufficient efficacy).

Table 1. Treatment Plans That Integrate Two Types of Therapies

Type of Treatment 1	Type of Treatment 2	Efficacy	Additional Notes
GVAX	Ipilimumab	Increased survival rate (compared to ipilimumab alone) (2)	-
Napabucasin (stem cell inhibition)	Gemcitabine and nab-paclitaxel	Greater than 35% objective response (survival rate: 10.7 months) (2)	-
Stereotactic body radiotherapy	IL-12	Increase in CD8 T cell activation, leading to marked tumor reduction (5)	Preclinical mice studies
	CCX872-B	Discontinued (5)	-
	Anti-PD1	Poorer survival outcomes as a result of lymphocyte depletion (22)	-
Irreversible electroporation	Anti-PD1	Inhibited tumor progression and extended lifespan of immunocompetent mice with PDAC (5)	Preclinical mice studies
	M1-oncolytic virus	Enhanced T-cell activation in the zinc-associated protein-deficient situation (5)	Preclinical mice studies

Continuation of Table 1.

Type of Treatment 1	Type of Treatment 2	Efficacy	Additional Notes
Irreversible electroporation	Intratumoral Toll-like receptor-7 agonist and PD-1 blockade	Enhanced therapeutic outcomes (5)	-
	Natural killer cell infusion	Dose-dependent objective response. However, no impact on survival rate was observed. This therapy regimen was connected to higher levels of serum IL-2, TNF-β, and IFN-γ (compared to the IRE group after treatment) (5)	All of these comparisons were calculated as clinically significant (P<0.05).
	Anti-PDL1 (Nivolumab)	An increase in effector memory cells was noted. However, a majority of the patients experienced grade ≥3 AEs (5)	
	Anti-PD1 (Toripalimab)	The progression-free survival was calculated as 10.6 months (compared to 27.5 months for IRE alone). Furthermore, the overall survival seems to be increasing (44.3 months compared to 23.4 months for IRE alone). Notably, the number of CD4+ and CD8+ T cells also increased, while the number of CD8+ Treg cells decreased (compared with those in the IRE-only treatment group) (5)	
Anti-PDL1	CXCR4 inhibitor (Plerixafor)	Studies observed an escalation on within-tumor CD3-positive T-cells and an induced tumor regression in KPC mice (13)	Preclinical mice study
Anti-CTLA4 (Ipilimumab)	Gemcitabine and nab-paclitaxel	No response (13). Other studies showed partial response in metastatic forms of pancreatic cancers in a minority of patients (12)	
CD-40 agonist (CP-870893)	Gemcitabine	Study in early stage (13)	-
Indoleamine-2,3-dioxygenase (IDO) inhibitor (Indoximod)	Gemcitabine and nab-paclitaxel	Ongoing phase Ib clinical trial. In preclinical trials, IDO inhibitors demonstrated high anti-cancer activity by increasing T-cell activity (13)	-
5-fluorouracil, leucovorin, oxaliplatin	PEGylated human IL-10 (AM0010)	Poor results were recorded with 15% total objective response (n=20). The median progression-free survival for these patients was only 3.9 months, while the patients experienced severe grade 3 and 4 AEs such as thrombocytopenia, anemia, and neutropenia (8)	-
OK432-pulsed DCs (intratumor), lymphokine-activated killer cells stimulated with anti-CD3 monoclonal antibody (intravenous infusion)	Gemcitabine	The phase I clinical trial provided promising results as 20% showed partial response and another 40% more than six months (n=5) (23)	-
Anti-PD1	IFN-γ	(With the requirement of delayed anti-PD1 treatment) showed significant anti-tumor effects (24)	-
Anti-CD40	Gemcitabine	Studies revealed that this combination is modifying the tumor stroma, inducing T cell-mediated anti-tumor activity, and reprogramming TAMs to exhibit tumoricidal properties.	-
A-emitting radioisotopes	Monoclonal antibodies	Studies showed a strong impact on in vitro studies and a tumor growth delay in vivo studies (25)	-

IL-12=Interleukin-12; anti-PD1=Anti-programmed cell death protein 1; IL-2=Interleukin-2; TNF-β=Tumor necrosis factor beta; IFN-γ=Interferon gamma; PD-1=Programmed cell death protein 1; anti-PDL1=Anti-programmed death ligand 1; IRE=Irreversible electroporation; CXCR4=C-X-C motif chemokine receptor 4; anti-CTLA4=Anti-cytotoxic T-lymphocyte-associated protein 4; CD-40=Cluster of differentiation 40; IL-10=Interleukin-10; AEs=Adverse events; DCs=Dendritic cells; anti-CD3=Anti-cluster of differentiation 3; TAMs=Tumor-associated macrophages; KPC=KrasLSL-G12D/+;Trp53R172H/+; Pdx1-Cre cells; CD3=Cluster of differentiation 3; CD4=Cluster of differentiation 4; CD8=Cluster of differentiation 8.

Conclusion

LAPC continues to be one of the most lethal forms of cancer, as evidenced by its dismal prognosis. Regrettably, the numerous studies referenced earlier have reported only marginal improvements in survival rates regarding immunotherapy options for LAPC, either yielding disappointing outcomes or presenting significant adverse effects in many participants involved in these clinical trials. Nonetheless, certain studies have revealed promising results through the application of specific therapeutic agents. This category includes various immune checkpoint inhibitors, such as anti-PD1, anti-PD-L1, and anti-CTLA4 agents, as well as CCR, CXCR2, and IDO inhibitors. Comparable effects have been observed in several vaccine trials, notably the GVAX vaccine when employed in combination therapies, alongside the FAP vaccine and the mKRAS-specific amphiphile vaccine, which showed encouraging results in patients harboring KRAS mutations. Furthermore, some of the most promising outcomes have been reported in CAR T-cell therapies, with mesothelin and carcinoembryonic antigens serving as primary targets, along with notable mentions of radioimmunotherapy trials. Although these therapies have demonstrated highly favorable results, there remains an urgent need for further investigation into the role of immunotherapy in the treatment of LAPC.

What Is Already Known on This Topic:

Locally advanced pancreatic cancer (LAPC) is a notable category of pancreatic cancer, characterized by a dismal prognosis and restricted treatment alternatives. Traditional treatment methods, such as chemoradiotherapy, are coming under scrutiny. Consequently, there is a pressing demand for the advancement of innovative strategies, the discovery of new pharmaceuticals, and further research in this area, including immunotherapy.

What This Study Adds:

Unfortunately, many of the studies mentioned previously have indicated only slight enhancements in survival rates associated with immunotherapy for LAPC, often resulting in unsatisfactory outcomes or notable adverse effects among numerous participants in these clinical trials. However, some studies have shown encouraging results with the use of particular therapeutic agents. Despite the positive findings of these therapies, there is a pressing need for additional research to explore the potential of immunotherapy in the treatment of LAPC.

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