A Systematic Review of Chemotherapeutic Regimens used in Pancreatic Cancer

Nimra Awaş 1, Travis Satnarine 2, Areeq Ahmed 1, Ayesha Haq 3, Deepkumar Patel 3, Grethel N. Hernandez 5, Kofi D. Seffah 8, Mustafa Abrar Zaman 9, Safeera Khan 11

1. Research, California Institute of Behavioral Neurosciences & Psychology, Fairfield, USA 2. Pediatrics, California Institute of Behavioral Neurosciences & Psychology, Fairfield, USA 3. Internal Medicine, California Institute of Neuroscience, West Hartford, USA 4. Internal medicine, California Institute of Behavioral Neurosciences & Psychology, Rawalpindi, PAK 5. Family medicine, California Institute of Behavioral Neurosciences & Psychology, Fairfield, USA 6. Internal Medicine, California Institute of Behavioral Neurosciences & Psychology, Los Angeles, USA 7. Internal Medicine, California Institute of Behavioral Neurosciences & Psychology, Athens, Georgia, USA 8. Internal Medicine, Piedmont Athens Regional Medical, Athens, USA 9. Internal Medicine, California Institute of Behavioral Neurosciences & Psychology, California, USA 10. Internal Medicine, St. George’s University School of Medicine, Newcastle Upon Tyne, GBR 11. Internal Medicine, California Institute of Behavioral Neurosciences & Psychology, Fairfield, USA

Corresponding author: Nimra Awaş, nimra_tehzib04@yahoo.com

Abstract
Pancreatic cancer is a malignant tumor with one of the worst prognosis. Its incidence has been on the rise in recent years. First line and second line treatments as well as adjuvants therapies have been employed in clinical trials for pancreatic cancer along with traditional chemotherapy and radiotherapy that has been enhanced. The prognosis of pancreatic ductal adenocarcinoma (PDAC) is still quite bad despite recent improvements in diagnostic and treatment methods. Since most patients are not candidates for treatment with a curative purpose, effective palliative care is crucial. For this systematic review, between December 25, 2022, and January 5, 2023, we searched PubMed, Medline, Cochrane, and Science Direct and discovered 225 relevant articles. The appropriateness of the literature abstracts for the pooled analysis was evaluated using different combinations of keywords such as pancreatic cancer, first- and second-line chemotherapy, palliative chemotherapy, Gemcitabine, Nab-Paclitaxel (GnP) AND Folfirinox (FFX). Eight research studies with 15236 people total, including systematic reviews, meta-analyses, and randomized controlled trials were included.

The only treatment choice for patients without metastatic disease who have clinical staging that suggests resectable or borderline resectable pancreatic cancer should be resection. This research examined how first- and second-line chemotherapeutic regimens (using different drug combinations) affected patients with locally advanced or borderline resectable pancreatic cancer and how they responded in terms of overall survival, tumor resectability, and progression-free interval. The review concludes by highlighting the results of these therapies. Notably, a growing body of research indicates that the two most popular first line medication combinations gemcitabine plus nab-paclitaxel (GnP) and Folfirinox (FFX), have similar results in RCTs and in real world populations. Results of second line therapy after first line regime failure are still dismal, and there is still a great deal of doubt regarding the best course of action. More RCTs and real-world evidence studies that address current and innovative regimens, as well as the best order in which to administer them, are required, with a greater emphasis on targeted therapy with fewer side effects.

Introduction And Background
In 2017, there were 447,665 new cases of pancreatic cancer reported worldwide (58.6 per million), with a prevalence of 49.8 per million and 441,083 fatalities (57.7 per million). Only patients who can undergo a complete resection have a chance of cure [1]. For patients who have metastatic disease, median survival is often less than half that when disease is unresectable due to invasion into important arterial structures. Although 5% to 10% of individuals have either a significant family history of pancreatic cancer, a recognizable mutation that increases risk, or both, most pancreatic tumors lack a genetic predisposition. Chronic pancreatitis, obesity, type 2 diabetes, excessive consumption of red meat, alcohol abuse, and smoking are risk factors. Palliative systemic therapy and/or radiotherapy are the sole available treatments for patients as well as for those resected patients who experience relapses [1].

Neoadjuvant chemotherapy (NAC) has been utilized to raise the R0 resection rate and transform locally progressed, unresectable cancers into tumors that may be resectable as a result of the recent development of more effective chemotheraphy regimens [2]. Additionally, NAC benefits patients by treating early micro metastatic illness, enhancing survival rates, and choosing poor responders who advance on treatment prior
to surgery, sparing them from a pointless procedure. According to these factors, various studies have shown that NAC is superior to initial surgery for patients with locally advanced and borderline resectable pancreatic cancer (BRPC) and LAPC. As a result, the National Comprehensive Cancer Network (NCCN) also suggests NAC as a conventional treatment for BRPC and LAPC [2].

In the past, 5-fluorouracil (5-FU)-based regimens were the only options for palliative therapy of PDAC, and they typically produced at best minimal outcomes. However, evidence from a randomized study conducted in 1996 revealed that palliative chemotherapy in PDAC increased median overall survival (MOS) as well as quality of life when compared to the best supportive care alone [3]. At the time, 5-FU treatment was more or less experimental. Based on the findings of a subsequent randomized trial with prolonged MOS in favor of gemcitabine [4], gemcitabine took the position of 5-FU as the industry standard in this clinical scenario the following year. In this study, we'll contrast how this regimen affects patients with BRPC and LAPC. When compared to single-agent gemcitabine, multi-agent regimens like Folfirinox and GNP have demonstrated considerable benefits. When compared to gemcitabine alone, both regimens had survival times that were twice as long and response rates of about 30% [4].

Combination therapy’s success will be aided by improving our knowledge of pancreatic cancer’s molecular basis and discovering more potent, targeted systemic treatments [5]. Enhancing prevention tactics and early identification can help the surgical outcomes as we work to overcome the formidable challenge of pancreatic cancer. Likewise, combination therapy, such as standard therapy (surgery, radiotherapy, or chemotherapy) combined with target therapy and immunotherapy, should also show favorable outcomes in the treatment of pancreatic cancer [4-5].

The purpose of this research was to compare the current treatments for (first line and second-line GEM/GEM-based regimes) borderline or locally advanced metastatic pancreatic cancer. We focused on overall survival (OS) as primary outcome, progression-free survival (PFS) and resection rate of tumor (R0) as secondary outcomes, after receiving these therapies. Additional research is needed with regard to the side effects of these chemotherapeutic medications and targeted therapy with fewer effects, that can produce more encouraging gains.

**Review**

This systematic review was conducted using the preferred reporting items for systematic review and meta-analysis (PRISMA) 2020 guidelines [6].

**Search sources and strategy**

We searched PubMed, Cochrane library, Medline, ScienceDirect for relevant literature. Various combinations of keywords like chemotherapy, pancreatic cancer, palliative chemotherapy, first- and second-line chemotherapy, gemcitabine AND Fluro-uracil were used to search all databases. In PubMed along with these keywords following strategy was used for relevant search.


Table 1 summarizes the databases used and the number of articles identified from that database.
**Inclusion Criteria and Exclusion Criteria**

We incorporated the latest publications and articles published in the past five years, including papers written in the English language. We only included research papers involving human participants with diagnosed borderline or locally advanced pancreatic cancer. If the entire contents of a research paper could not be accessed, it was excluded. A list of our inclusion and exclusion criteria is shown in Table 2.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>1-Papers written and published in the English language in the past five years.</td>
<td>1-Grey literature</td>
</tr>
<tr>
<td>2-Type of intervention: Any form of chemotherapy, any combination of chemotherapy and radiotherapy, best supportive care, or another chemotherapy and/or radiotherapy treatment plan. Papers focusing on patients with pancreatic cancer who received gemcitabine, fluorouracil (as first and second line) with borderline or locally advanced pancreatic cancer.</td>
<td>2-Papers written and published in languages other than English.</td>
</tr>
<tr>
<td>3-Research papers involving human participants</td>
<td>3-If the complete text of the papers could not be retrieved, articles were excluded.</td>
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</table>

**TABLE 2: Inclusion and exclusion criteria**

**Characteristics of participants**

People with a diagnosis of pancreatic adenocarcinoma established by either histological or cytological findings (investigations on body tissue or cells). Studies enrolling people with advanced, unresectable or recurrent disease were eligible for inclusion.

**DATA EXTRACTION**

After comprehensive article review and extract, primary (overall survival) and secondary outcomes (progression free survival and tumor resection rate) were evaluated. NA independently extracted data using a specified form.

**Selection Process**

After eliminating the duplicate papers, we moved the articles to the Endnote. Titles and abstracts were used to screen each article by NA (the first author independently). Only pertinent articles were analyzed when the entire texts of the shortlisted articles were assessed. Only articles that met the inclusion and exclusion criteria were given a chance to be shortlisted.
Quality Assessment of Studies

We used assessment of multiple systematic reviews (AMSTAR) checklist for systematic reviews and meta-analysis and Cochrane risk of bias tool used for RCTs to assess the risk of bias.

Data Collection Process

Following finalization of the articles for the systematic review and extraction, the primary outcomes and other pertinent data were evaluated. The data was separately collected by NA, and the following details were gleaned: authorship, publication year, study design, study objective population, intervention employed, result, and conclusion.

Results

A total of 2270 publications were gathered via PubMed, Medline, ScienceDirect, and Cochrane Library. There were 90 articles left after the duplicates were removed, and they were filtered according to the inclusion and exclusion criteria. After the screening and eligibility, only 8 pertinent journal articles remained. An overview of the PRISMA flow chart is shown in Figure 1.

![PRISMA flowchart illustrating article selection process](https://assets.cureus.com/uploads/figure/file/629330/article_river_6b713f80ee7d11edac31a963047f536-IMG-20230509-WA0056-1-.png)

**FIGURE 1:** PRISMA flowchart illustrating article selection process [6].

Reason 1=paper was irrelevant.
Reason 2=unable to access the paper.
Reason 3= did not satisfy inclusion criteria.

MESH, medical subject heading;PRISMA, Preferred Reporting Items for Systemic Reviews and Meta-Analysis

Study identification and Selection

Eight published journal articles that included 15236 patients underwent thorough selection analysis. There were Four randomized clinical trials and four systematic reviews and meta-analyses. The pertinent articles included in this review are summarized in table 3 below. The patient’s health, illness stage, drug adverse effects, prior chemotherapeutic treatment, and resistance to it are all important considerations when choosing the regimen.

<table>
<thead>
<tr>
<th>Author and year of publication</th>
<th>Type of study</th>
<th>No. of participant</th>
<th>Drugs used</th>
<th>Result</th>
<th>Conclusion</th>
</tr>
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<tr>
<td>Dong L. P et al., 2022 [2]</td>
<td>Systematic review and Meta-Analysis</td>
<td>1351</td>
<td>Folfirinox, gemcitabine and Nab-paclitaxel.</td>
<td>Folfirinox had improved PFS and OS, a greater resection rate (including a R0 resection rate), and a lower rate of severe toxicity. Between the two groups, there are no differences in the rates of stable disease or partial/complete regression.</td>
<td>In comparison to the GNP group, the Folfirinox group reported higher resection and R0 resection rates as well as superior PFS and OS results for patients with BRPC and LAPC. Compared to GNP, there was no higher rate of</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Study Type</td>
<td>Study Design</td>
<td>Participants</td>
<td>Outcomes</td>
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<tr>
<td>Citterio et al., 2018</td>
<td>Meta-analysis</td>
<td>1587</td>
<td>IRI, FP, folinic acid (FA) and OXA. Irinotecan, fluoropyridine, cisplatin, oxaplatin</td>
<td>In terms of FP and OXA-FP, in particular, the combination IRI-FP-FA outperformed all other therapies in terms of OS and PFS.</td>
<td></td>
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<tr>
<td>Se-II Go et al., 2021</td>
<td>Randomized controlled Trial</td>
<td>80</td>
<td>MFOLFIRINOX, oxaliplatin, irinotecan, leucovorin, 5-FU infusion</td>
<td>In the mFOLFIRINOX and S-1 groups, the median progression-free survival rates were 5.2 and 2.2 months. In the mFOLFIRINOX and S-1 groups, the median overall survival rates were 9.2 and 4.9 months. In the mFOLFIRINOX and S-1 groups, 56% and 17% of the patients experienced grade 3-4 adverse events.</td>
<td></td>
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<tr>
<td>Ana Acuna-Villaorduña et al., 2022</td>
<td>Clinical Trial</td>
<td>22</td>
<td>FOLFIRINOX, gemcitabine-based chemoradiation</td>
<td>18 of the 22 patients received. In patients who had at least 1 cycle of FOLFIRINOX, the bias corrected R0 rate was 55.6%, and in patients who underwent surgery, it was 80%. The OS had a median of 35.1 months. 34 months was the median PFS for patients who underwent surgery.</td>
<td></td>
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<tr>
<td>Fietkau R et al., 2020</td>
<td>Randomized Trial</td>
<td>180</td>
<td>Gemcitabine, folfirinox chemoradiotherapy</td>
<td>126/180 individuals who underwent induction chemotherapy were randomly assigned to receive further treatment. 36 of the 126 individuals who received trial therapy underwent surgery. Patients with R0 resected tumors had significantly higher disease-free survival (DFS) and overall survival (OS) rates than non-operated patients.</td>
<td></td>
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<tr>
<td>Assenat.E</td>
<td></td>
<td></td>
<td></td>
<td>In 3.5% of patients, the tumor completely responded, in 61.4% it only partially responded. Sequential AG and FFX demonstrated acceptable toxicity as first-line therapy with no serious toxicity for Folfirinox.</td>
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Patients who had not previously received treatment with IRI-FP. Folionic Acid may benefit from overall survival when used as a second-line treatment for metastatic pancreatic cancer.

For mPAC patients resistant gemcitabine-based chemotherapy, the administration of mFOLFIRINOX as a second-line chemotherapy treatment led to higher survival rates than S-1 treatment alone.

High R0 resection rates were achieved in patients undergoing surgery when a multimodality treatment combining FOLFIRINOX, gemcitabine, and radiation was used.

After receiving neoadjuvant therapy, pancreatic cancer tumour resectability that was staged as unresectable at original diagnosis should be reevaluated. If a resectability is established, surgery should be performed on the patient because it vastly improves their prognosis.
responded, and in 19.3% of patients it progressed. The median progression-free survival and overall survival were 15.1 months and 10.5 months, respectively. Limiting neurotoxicity, while demonstrating high response and survival rates. No significant advantage of one regimen over the other in terms of overall risk of death and progression, despite FOLFIRINOX having a longer median OS compared to GEM-NAB.

The mean weighted OS difference was in favor of FOLFIRINOX by 1.15 months. Between the two arms, PFS did not differ. When compared to GEM-NAB and FOLFIRINOX, the total response rate was comparable (25 vs. 24%). As compared to FOLFIRINOX, GEM-NAB had less neurotoxicity and anemia while FOLFIRINOX had less nausea, neutropenia, and febrile neutropenia.

The long-established standard of care, gemcitabine, has recently been replaced by combination chemotherapy. It is quite effective to combine FOLFIRINOX with gemcitabine and nab-paclitaxel. Clinicopathological categorization is still tricky, which makes choosing the best treatment for certain patients challenging. To assist patients in making informed treatment decisions, biomarker discovery is crucial.

### TABLE 3: Summary of the studies included.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Patients</th>
<th>Treatment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>et al., 2021</td>
<td>Clinical Trial</td>
<td>91</td>
<td>Gembrax (Nab-paclitaxel, Gemcitabine) Folfirinox</td>
<td>responded, and in 19.3% of patients it progressed. The median progression-free survival and overall survival were 15.1 months and 10.5 months, respectively. Limiting neurotoxicity, while demonstrating high response and survival rates.</td>
</tr>
<tr>
<td>Pusceddu.S et al., 2019</td>
<td>Systematic Review and Meta-analysis</td>
<td>3813</td>
<td>GEM-NAB and FOLFIRINOX</td>
<td>The mean weighted OS difference was in favor of FOLFIRINOX by 1.15 months. Between the two arms, PFS did not differ. When compared to GEM-NAB and FOLFIRINOX, the total response rate was comparable (25 vs. 24%). As compared to FOLFIRINOX, GEM-NAB had less neurotoxicity and anemia while FOLFIRINOX had less nausea, neutropenia, and febrile neutropenia.</td>
</tr>
<tr>
<td>Chin.v et al., 2018</td>
<td>Systematic Review</td>
<td>9463</td>
<td>5FU, FOLFIRINOX, Gemcitabine, platinum, Topoisomerase inhibitor, nab-paclitaxel, gemcitabine incorporating (GEMOXEL or cisplatin/epirubicin/5FU/gemcitabine)</td>
<td>SFU reported lower OS, PFS, and QoL compared to gemcitabine alone. In terms of OS, PFS, and response rates, FOLFIRINOX outperformed gemcitabine, but it was associated with more adverse events. When compared to bolus dosage, gemcitabine administration at a fixed dose rate improved OS but increased the rate of adverse events. As compared to gemcitabine alone, combinations with platinum enhanced PFS and response rates but not OS. The frequency of adverse reactions grew. Fluoropyrimidine added to gemcitabine enhanced OS, PFS, and response rates but significantly raised adverse effects. Topoisomerase inhibitor plus gemcitabine did not boost survival rates but did increase toxicity. The combination of gemcitabine and nab-paclitaxel enhanced side effects while improving OS, PFS, and response rates. OS, PFS, and QOL were all improved by multidrug regimens incorporating gemcitabine (GEMOXEL or cisplatin/epirubicin/5FU/gemcitabine).</td>
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The shortlisted articles were evaluated for quality assessment using the relevant techniques. The Cochrane Bias Assessment Tool was used to evaluate Randomized Controlled Trials, while the Assessment of Multiple Systematic Reviews (AMSTAR) Checklist was used to evaluate Systematic Reviews and Meta-Analysis. The quality assessment used to evaluate study bias are shown in Tables 4 and 5.

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<td>Q1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</table>
TABLE 4: AMSTAR Checklist for a Systematic Review and Meta-analysis.

AMSTAR, A Measurement Tool to assess Systematic Reviews

Q1 - Did the research questions and inclusion criteria for review include the components of PICO?

Q2 - Did the report of the review contain an explicit statement that review methods were established prior to conduct of review and did the report justify any significant deviations from the protocol?

Q3 - Did the review authors explain their selection of the study designs for inclusion in the review?

Q4 - Did the review authors use a comprehensive literature search strategy?

Q5 – Did the review authors perform study selection in duplicate?

Q6 - Did the review authors perform data extraction in duplicate?

Q7 - Did the review authors provide a list of excluded studies and justify the exclusions?

Q8 - Did the review authors describe the included studies in adequate detail?

Q9 - Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

Q10 - Did the review authors report on the sources of funding for the studies included in the review?

Q11 - If meta-analysis was performed, did the review authors use appropriate methods for statistical combinations of results?

Q12 - If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

Q13 - Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?

Q14 - Did the review authors provide a satisfactory explanation for and discussion of any heterogeneity observed in the results of the review?

Q15 - If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?

Q16 - Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
Study Type (RCT) | Selection bias (randomization process) and (allocation concealment) | Performance bias | Detection bias | Attrition bias | Reporting bias | Other bias
--- | --- | --- | --- | --- | --- | ---
Se-Il Go et al., 2021 [7] | Yes, Yes | No | No | Yes | Yes, unclear |
Ana Acuna-Villaorduna et al., 2022 [9] | Yes, unclear | No | unclear | Yes | Yes, No |
Fietkau. R et al., 2020 [10] | Yes, Yes | No | Yes | Yes | Yes, No |
Assenat E et al., 2021 [11] | Yes, Yes | Yes | Yes | Yes | Yes, unclear |

TABLE 5: Shows risk bias assessment for RCTs.
RCTs, randomized controlled trials.

Discussion
One of the most challenging cases for medical oncologists worldwide continues to be pancreatic cancer that cannot be surgically removed. Although diagnostic imaging tools have improved, the majority of cases are still discovered at a stage when there is no chance of recovery or long-term survival. But there are valid grounds for cautious hope [5-6].

In this study, we review the outcomes of clinical trials and observational studies that discuss various chemotherapy regimens, used in patients with locally advanced or borderline pancreatic cancer and how those patients respond in terms of overall survival, progression-free time, and resection rate following chemotherapy.

First and Second line Therapy
The first-line therapy has been the subject of numerous studies, while research on the second-line is still scarce. For the best-performing patients, the FOLFIRINOX regimen combining 5-fluorouracil (5-FU), Oxaliplatin (OXA), Irinotecan (IRI), and folinic acid is used as an alternative to the standard first-line regimens of combinations of Gemcitabine (GEM) based chemotherapy, such as GEM + Nab-paclitaxel (FA).

Making a decision between these two regimens presents a difficult dilemma because, in order for patients to receive second-line chemotherapy, the option is premised on their prior treatment [7]. This information is summarized in figure 2.

Irinoeten-containing treatment plans (IRI-FP-FA, IRI-FP, and IRI) were the most successful therapy combinations when it came to treating OS. IRI-FP-FA was the best treatment in terms of PFS, followed by OXA-FP-FA plus IRI. The OXA-FP and FP combination had the lowest outcomes in this scenario [7].

Due to its invasive biological properties, chemotherapy is the cornerstone of advanced PC. The selection of the First-line therapy for MPC is influenced by wide range of variables. Relapse free survival (RFS) duration is important in deciding between the two treatments, in case of relapse following adjuvant gemcitabine or gemcitabine-based therapy, with GEM-NAB only being useful in cases of patient relapse occurring after 6 months. Since triplet therapy has a higher toxicity profile than GEM-NAB, the decision to use FOLFIRINOX is primarily based on the health of the patient. Additionally, hospitalization for supportive care, the use pegfilgrastim, and the cost of anti-emetics associated with FOLFIRINOX toxicity should all be taken into account.
Although immunotherapy has seen a therapeutic resurgence in recent years for many solid tumors, cells by overcoming the processes through which malignancies thwart and suppress immune responses. Immunotherapy aims to improve or restore the immune system’s capacity to recognize and eliminate cancer by triggering, enhancing, or reducing the immune system’s response, treating disease. Cancer immunotherapy for pancreatic cancer is a realistic alternative. For patients with borderline or locally advanced pancreatic cancer, multi-agent chemotherapy regimens like Folfirinox and gemcitabine plus nab-paclitaxel have demonstrated considerable benefits when compared to single-agent gemcitabine. It is still debatable if Folfirinox and gemcitabine plus nab-paclitaxel are effective and safe NACs for BRPC and LAPC.

Folfirinox outperformed gemcitabine in terms of resection rate and R0 resection rate, PFS and OS, and severe toxicity rate while having greater resection rates overall. There are no differences between the two groups in the rates of stable disease or partial/complete regression. For patients with BRPC and LAPC, the Folfirinox group outperformed the GNP group in terms of resection and R0 resection rates, as well as PFS and OS outcomes. When compared to gemcitabine, Folfirinox did not exhibit a higher rate of serious toxicity. The GABRINOX (AG followed by FFX) response rate, safety, and efficacy were evaluated in a phase Ib–II trial in 2021. AG was administered sequentially, and it was hypothesized that targeting the tumor microenvironment with nab-paclitaxel would improve FFX access to the tumor and, consequently, its efficacy. In addition to a higher survival rate, this phase Ib–II research demonstrated high response rates, acceptable tolerability, and no neurotoxicity.

Role of Multimodality therapy

In patients with BR-PDAC, a sequential multimodality therapy consisting of induction FOLFIRINOX, concurrent gemcitabine, and radiation showed good effectiveness with a R0 resection rate of 55.6% and was well tolerated. As 68.2% of the enrolled patients were able to undergo surgery, this regimen demonstrated a favorable balance between efficacy and tolerance; the other patients were unable to tolerate the treatment or developed metastatic illness. Another indicator of effectiveness is the high rate (80%) of patients having surgery with R0 margins, with 100% of them being recurrence-free after one year. Despite the R0 resection rate, this regimen is effective because the median OS is close to 3 years and the 1-year OS rate is 85.1% across all trial participants.

Phase 2 of an incremental multimodality regime investigation was conducted, based on 22 individuals with tumors that had metastases in four or more regional lymph nodes and were limited to the pancreas head and neck, induction FOLFIRINOX was utilized in conjunction with concurrent gemcitabine and radiotherapy in patients with BR-PDAC. Given that the trial’s accrual goal was not met, the fact that this resection rate fell short of the threshold for statistical significance could have been a factor. After neoadjuvant therapy, tumor resectability should be evaluated if pancreatic cancer was staged as unresectable at the time of the first diagnosis. Surgery should be performed on individuals with a high probability of R0 resection if they are in good enough health since it considerably improves their prognosis. Therefore, the notion of treatment for these patients should include surgery as a potential option. The technologies used today (CT and MRI) to determine the resectability of pancreatic cancer are not always accurate at predicting R0 resectability. In order to enhance R0 resectability assessments, new approaches must be sought after.

Adverse Effects

The course of treatment may be impacted by unfavorable consequences of chemotherapy. The two arms were compared for adverse events (AEs) of grade 3-4 (G 3–4) with hematological and non-hematological toxicities. In the GEM-NAB arms, neutropenia and febrile neutropenia were significantly reduced. As opposed to FOLFIRINOX, GEM-NAB treatment was more frequently associated with G 3–4 anemia. Only nausea and neurotoxicity showed a statistically significant difference between the two arms among non-hematological effects (90% less nausea and 2.5 times higher neurotoxicity with GEM-NAB as compared with FOLFIRINOX). Treatment time was comparable across GEM-NAB and FOLFIRINOX, lasting three (monthly) cycles as opposed to 5.4 (biweekly). There were no reports of toxic fatalities, dose reductions, or therapy halts. The moderate benefit of these regimens should be weighed against the potential side effects, and for patients in poor general health, best supportive care should be considered as a realistic alternative.

Immunotherapy for pancreatic cancer

By triggering, enhancing, or reducing the immune system’s response, immunotherapy treats disease. Cancer immunotherapy aims to improve or restore the immune system’s capacity to recognize and eliminate cancer cells by overcoming the processes through which malignancies thwart and suppress immune responses. Although immunotherapy has seen a therapeutic resurgence in recent years for many solid tumors,
pancreatic cancer, one of the most immune-resistant tumor forms, did not show any substantial benefit with immunotherapy alone. Yet, there is still hope for effective treatments for pancreatic cancer, particularly for metastatic pancreatic cancer that is resistant to all current therapy. Vaccination, adoptive immunization, and immunological checkpoint blockade are currently the mainstays of pancreatic cancer immunotherapy [14].

The main limitation of our study is the modest number of studies we included in our network, comparing different chemotherapy regimens for pancreatic cancer.

Conclusions

The outcomes of this study imply that using multiple medication regimens for advanced PC may optimize outcomes. Additionally, there are numerous chemotherapies that can be selected based on patients clinicopathological backgrounds. In both the first line and, to a lesser extent, the second-line settings, a number of multidrug regimens have encourages potency and tolerable toxicity. When the corresponding regimens are given to patients in real-world settings, the outcomes reported in RCTs appear to be very consistent.

Improving preventative tactics and early identification is crucial to enhancing surgical results in the fight against the formidable challenge of pancreatic cancer. Combination therapy, such as standard therapy (surgery, radiotherapy, or chemotherapy) combined with immunotherapy and target therapy, should also be effective in the treatment of pancreatic cancer. The success of combination therapy will be aided by improving our knowledge of the molecular basis of pancreatic cancer and discovering more potent, individualized systemic medicines. Therefore, more research in the fields of targeted and immunotherapy is required to achieve promising results in the future.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References