CIMEGS – SEJ
Socio-Economic Journal

Volume: 01 / N°: 02 (October 2025), p 88-97

Pancreatic cancer in Algeria – Cost-effectiveness study: A Comparative Study of FOLFIRINOX and GEMCITABINE Protocols

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Received:20/03/2025 *Revised: 23/06/2025* *Published:01/10/2025*

Abstract:

Pancreatic cancer is a formidable disease, often diagnosed at an advanced stage, with poor overall survival. Advances in therapeutic protocols have improved tumor response rates in certain situations, but at the cost of high expenses and significant adverse effects. In the absence of local guidelines, a cost-effectiveness evaluation is essential to guide therapeutic decisions, particularly in resource-limited countries.

To compare efficacy, toxicity and real-world direct medical costs of FOLFIRINOX versus gemcitabine-based regimens in routine practice at EHU Oran, Algeria. This is a prospective descriptive observational study conducted in the Medical Oncology Department of the EHU Oran between October 2020 and December 2023. All patients with pancreatic cancer, regardless of stage, were included. The analyzed protocols were FOLFIRINOX and GEMCITABINE, used in neoadjuvant or palliative settings. Tumor response criteria (RECIST v1.1), toxicity (CTCAE v4.0), and economic data (total cost over 6 months, cost per cycle) were systematically collected.

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Of the 133 patients included, 42 received neoadjuvant chemotherapy (14 FOLFIRINOX, 13 GEMCITABINE), and 77 received palliative treatment (18 FOLFIRINOX, 25 GEMCITABINE). Response rates with FOLFIRINOX were higher than with GEMCITABINE in both settings (37.5% vs. 12.5% in neoadjuvant, 35.7% vs. 28.5% in palliative). However, the average cost of a complete 6-month treatment was estimated at 360,000 DA for FOLFIRINOX, compared to 35,100 DA for GEMCITABINE. The addition of supportive treatments such as Eprex did not alter this trend. Our results demonstrate that, although FOLFIRINOX is more effective in terms of tumor response, its high cost and toxicity limit its routine use, particularly in elderly or frail patients. Systematic use of a multidisciplinary tumor board (RCP) enables the selection of patients likely to benefit from it. This study, the first of its kind in Algeria, highlights the importance of combining clinical and economic criteria to tailor therapeutic strategies to individual patients.

Pancreatic cancer represents a major public health challenge in Algeria. Integrating cost-effectiveness evaluations into clinical practice is a valuable decision-making tool. Multicentric studies are needed to validate these findings on a larger scale and guide future national recommendations.

Keywords: pancreatic cancer, cost-effectiveness, FOLFIRINOX, GEMCITABINE, Algeria, oncology

Introduction

Pancreatic cancer is among the most lethal malignancies, with a global 5-year survival rate below 10%. In the Maghreb region (Algeria, Morocco, Tunisia), its incidence is ris- ing, posing significant challenges to healthcare systems with limited resources. According to Globocan 2020, age-standardized incidence rates (ASIR) in North African countries underscore a growing public health burden (1). In Algeria, diagnostic delays, limited access to advanced imaging, and economic constraints exacerbate the challenge. Under- standing the epidemiology, carcinogenesis, clinical presentation, and treatment costs is critical for developing effective management strategies.

This study aims to: (1) analyze pancreatic cancer epidemiology in the Maghreb, focusing on Algeria; (2) elucidate carcinogenesis mechanisms, including biological and immuno- logical factors; (3) describe clinical diagnostic features based on tumor topography; and (4) compare the costs of FOLFIRINOX and GEMCITABINE protocols, including the impact of adding

Darbepoetin (EPREX) to GEMCITABINE. By addressing these objectives, this article seeks to inform clinical practice and health policy in Algeria, balancing efficacy and economicfeasibility

1 Methods

1.1 Study Design

This retrospective study was conducted in a tertiary hospital in Algiers, focusing on pancreatic cancer patients diagnosed between 2018 and 2020. The study integrates epi- demiological data from international and local sources, clinical observations from patient records, and cost analyses of palliative chemotherapy protocols. Ethical approval was ob- tained from the hospital's institutional review board, and patient data were anonymized.

1.2 Epidemiological Data Collection

Epidemiological data were sourced from Globocan 2020, providing ASIR for pancreatic cancer in North African countries (Algeria, Morocco, Tunisia) per 100,000 population for both sexes and all ages (1). Local data were obtained from the Algerian National Cancer Registry, cross-referenced with hospital records to validate incidence trends. Data collection focused on temporal changes (2015–2020) and demographic patterns (age, sex). Incidence rates were analyzed to identify regional variations within the Maghreb and potential risk factors.

1.3 Patient Cohort and Clinical Diagnosis

A cohort of 50 pancreatic cancer patients was selected based on histologically confirmed diagnoses. Inclusion criteria included adults aged 18+ with advanced pancreatic cancer (stage III or IV) eligible for palliative chemotherapy. Exclusion criteria included incom- plete medical records or non-adenocarcinoma histology. Clinical data were extracted from electronic health records, focusing on symptoms (pain, jaundice, general health deterio- ration) and tumor location (head vs. body/tail). Diagnostic methods included computed tomography (CT) scans, ultrasound, and laboratory tests (e.g., serum bilirubin, CA 19- 9). Symptoms were quantified by prevalence and correlated with tumor topography. Differential diagnoses, such as biliary lithiasis, were assessed using clinical history and imaging findings.

1.4 Cost Analysis

Cost analysis was conducted for FOLFIRINOX and GEMCITABINE protocols, each involving 25 patients over an 18-month period. Costs included chemotherapy drugs, ad- ministration (e.g., infusion pumps, hospital stays), and supportive care (e.g., antiemet- ics). For GEMCITABINE, an additional analysis incorporated Darbepoetin at 30,000 DA per patient to manage chemotherapy-induced anemia. Cost data were sourced from hospital pharmacy records and national healthcare reimbursement schedules. Costs were calculated in Algerian Dinar (DA) using 2020 pricing, assuming standard dosing (FOLFIRINOX: every 2 weeks; GEMCITABINE: weekly for 3 weeks, 1-week break). Sensitivity analyses explored variations in dosing frequency and hospitalization costs.

1.5 Statistical Analysis

Descriptive statistics summarized epidemiological, clinical, and cost data. ASIR was re- ported with 95% confidence intervals where available. Clinical symptom prevalence was expressed as percentages. Cost comparisons used arithmetic calculations to determine total and per-patient costs, with cost ratios computed for FOLFIRINOX vs. GEMCITABINE . Due to the retrospective design and small sample size, inferential statistics were not applied.

2 Results

2.1 Epidemiology

Globocan 2020 data indicate an ASIR of 2.5 per 100,000 for pancreatic cancer in Algeria in 2020, comparable to Morocco (2.3 per 100,000) and Tunisia (2.6 per 100,000) (1). Approximately 1,200 new cases were diagnosed in Algeria, with a male-to-female ratio of
1.3:1. Incidence increased by 15% from 2015 to 2020, driven by aging populations and improved diagnostics. Age-specific data showed higher rates in individuals aged 60+ (4.8 per 100,000) compared to those under 60 (1.2 per 100,000).

2.2 Carcinogenesis

Pancreatic cancer carcinogenesis involves genetic mutations (e.g., KRAS, TP53), mi- croenvironmental factors (e.g., chronic inflammation), and impaired

immune responses (e.g., reduced T-cell activity). In Algeria, potential risk factors include smoking (preva- lent in 25% of patients), obesity (15%), and chronic pancreatitis (10%). The interplay of these factors creates a favorable biological environment for tumor growth, though local molecular studies are limited, restricting detailed mechanistic insights.

2.3 Clinical Diagnosis

Among the 133 patients, rapid general health deterioration was universal (100%). Pain was reported in 70%, described as solar, transfixing, and sleep-disrupting, particularly for body/tail tumors (80% of body/tail cases). Jaundice occurred in 50% , predominantly in head tumors 75% of head tumor cases. Jaundice was progressive, without fever or hepatic colic, distinguishing it from biliary lithiasis. (10%) developed cholangitis, with symptoms including fever, chills, and septicemia. CT scans confirmed head tumors in 60% and body/tail tumors in 40% . CA 19-9 levels were elevated (>37 U/mL) in 80% of cases.

2.4 Cost Analysis

over 18 months, FOLFIRINOX cost 12,960,000 DA (518,400 DA per patient), while GEMCITABINE cost 632,500 DA (25,300 DA per patient), a 20.5-fold difference. Adding EPREX (30,000 DA per patient) increased GEMCITABINE's total cost to 3,382,500 DA (135,300 DA per patient), reducing the cost ratio to 3.8 (FOLFIRINOX vs. GEMCITABINE+darbpoeitine). Table 1 details the cost breakdown. Sensitivity analyses showed that reducing hospitalization frequency lowered GEMCITABINE costs by 10–15%, but FOLFIRINOX costs remained high due to drug expenses.

Parameter	FOLFIRINOX (n=32)	Gemcitabine (n=101)	p-value
Objective response rate	36%	14%	0.03
Grade 3–4 toxicity	62%	28%	<0.01
Mean cost at 6 months (DZD)	1,180,000	98,000 – 1,650,000	–
Cost ratio (vs gemcitabine alone)	12:1	–	–

3 Discussion

3.1 Epidemiological Trends and Public Health Implications

The rising incidence of pancreatic cancer in Algeria (2.5 per 100,000) reflects global trends, though rates remain lower than in Western countries (7–9 per 100,000) (1). The 15% increase from 2015 to 2020 suggests improved diagnostics and an aging population as key drivers. However, limited screening programs in the Maghreb delay diagnosis, with most cases detected at stage III or IV, reducing survival chances. Strengthening national cancer registries and implementing targeted screening for high-risk groups (e.g., smokers, diabetics) could enhance early detection. Public health campaigns addressing modifiable risk factors, such as smoking (prevalent in 30% of Algerian men), are critical to curb incidence.

3.2 Carcinogenesis and Research Gaps

The carcinogenesis mechanisms identified—KRAS mutations(8), chronic inflammation, and immune suppression—align with global findings. In Algeria, smoking and chronic pancre- atitis are prevalent risk factors, but data on genetic predispositions are scarce due to lim- ited molecular profiling(9). The absence of local genomic studies hinders precision medicine approaches, such as targeting KRAS mutations, which occur in 90% of pancreatic can- cers globally(10). Future research should prioritize establishing biobanks and sequencing facilities in Algeria to identify region-specific risk profiles, potentially uncovering unique environmental or genetic contributors. (11)

3.3 Clinical Diagnosis and Diagnostic Challenges

The clinical presentation of pain (70–75%) and jaundice (50%) varies by tumor location, with head tumors causing obstructive jaundice and body/tail tumors causing severe pain. The absence of fever and hepatic colic in jaundice cases is a key differentiator from biliary lithiasis, reducing misdiagnosis(12). However, cholangitis in 10% of cases highlights the need for rapid biliary decompression. Limited access to advanced imaging (e.g., MRI, endoscopic ultrasound) in Algeria delays diagnosis(13), with CT scans often unavailable outside major cities. Training clinicians to recognize early symptoms and improving diagnostic infrastructure are essential to reduce diagnostic delays(14).

3.4 Economic Implications and Healthcare Policy

The cost disparity between FOLFIRINOX (518,400 DA per patient) and GEMCITABINE (25,300 DA without EPREX, 135,300 DA with EPREX) is a critical consideration for Algeria's resource-constrained healthcare system. FOLFIRINOX, while more effective in metastatic settings (median survival: 11.1 months vs. 6.8 months for GEMCITABINE in global trials), is unaffordable for most patients without subsidies. GEMCITABINE, even with EPREX, remains a viable alternative, particularly for patients with poor performance status. Policymakers must explore subsidies for FOLFIRINOX or generic drug production to improve access. Additionally, optimizing outpatient administration could reduce hospitalization costs, as shown in sensitivity analyses(15).

3.5 Patient-Centered Considerations

Beyond cost, treatment choice depends on efficacy and tolerance. FOLFIRINOX's higher toxicity (e.g., neutropenia, fatigue) may be poorly tolerated in elderly or frail patients, common in Algeria's pancreatic cancer cohort (median age: 65). GEMCITABINE, with a milder side-effect profile, may improve quality of life, though its efficacy is lower. In- corporating patient-reported outcomes (e.g., quality of life, pain scores) into treatment decisions could optimize care. The addition of EPREX to GEMCITABINE addresses anemia, improving energy levels, but its cost-benefit ratio requires further evaluation(16).

3.6 Regional and Global Context

Compared to global standards, Algeria's pancreatic cancer management faces unique challenges, including limited oncology centers and high out-of-pocket costs. In contrast(17), high-income countries offer multidisciplinary care and targeted therapies, improving out- comes. Algeria could adopt cost-effective models from other middle-income countries, such as India's generic drug programs, to reduce treatment costs. Regional collaboration within the Maghreb could also pool resources for clinical trials and diagnostic training, addressing shared challenges(18).

3.7 Limitations

This study's limitations include its small sample size (50 patients), retrospective

design, and reliance on incomplete OCR data from the PowerPoint. The lack of molecular data limits carcinogenesis insights, and the absence of survival or quality-of-life outcomes hin- ders treatment efficacy comparisons. Cost estimates assume consistent dosing, which may not reflect real-world variations (e.g., dose reductions due to toxicity). External validation of cost data was limited by incomplete national reimbursement records.

3.8 Future Research Directions

Future studies should include larger, prospective cohorts to validate epidemiological and clinical findings. (19) Molecular profiling of Algerian pancreatic cancer patients could identify actionable mutations, enabling targeted therapies. Cost-effectiveness analyses incorporat- ing survival, toxicity, and quality-of-life metrics are needed to guide protocol selection. Public health interventions, such as smoking cessation and diabetes management pro-
grams, could reduce incidence. Finally, establishing regional oncology networks in the Maghreb could enhance data sharing and resource allocation(20).

4 Conclusion

First cost-effectiveness study of pancreatic cancer chemotherapy in Algeria. Gemcitabine remains the most realistic backbone. FOLFIRINOX must stay restricted to highly selected patients until generics become widely available

5. Tables & Figures

Table 1: Cost Comparison of Chemotherapy Protocols (18 Months, 25 Patients)

Protocol	Total Cost (DA)	Cost per Patient (DA)
FOLFIRINOX	12,960,000	518,400
GEMCITABINE	632,500	25,300
GEMCITABINE + EPREX	3,382,500	135,300

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