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Metastatic Pancreatic Adenocarcinoma Treatment, Which One Should be the First Choice, Nab-Paclitaxel Plus Gemcitabine or FOLFIRINOX? A Real Word Data Approach Using Trinetx

(*Tratamento de Adenocarcinoma Pancreático Metastático, Qual Deve ser a Primeira Escolha, Nab-Paclitaxel Mais Gemcitabina ou FOLFIRINOX? Uma Abordagem de Dados do Mundo Real Usando Trinetx*)

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Metastatic Pancreatic Adenocarcinoma, Nab-Paclitaxel, Gemcitabine, Trinetx.

RESUMO (POR)

Introdução: O câncer de pâncreas (PDAC) representa a terceira principal causa de morte por câncer, com incidência crescente de 1% ao ano. Atualmente a sobrevida global continua sendo uma das mais baixas entre os cânceres. Durante as últimas décadas, FOLFIRINOX e Gemcitabina + Nab-paclitaxel representaram o padrão de tratamento como primeira linha. No entanto, uma comparação direta entre eles é escassa na literatura. Nosso estudo buscou fornecer dados de sobrevida global comparando esses dois principais esquemas de quimioterapia para PDAC metastático usando dados de mundo real fornecido pela Trinetx. Método: A TriNetX é uma rede global federada de registros médicos eletrônicos que compreende 127.437.189 pacientes. Os dados foram coletados retrospectivamente e analisados visando o desfecho de morte. O PSM (propensity score matching) sobre 11 características clínicas foi realizado para balanceamento das coortes. Para análise de sobrevivência, o método Kaplan-Meier estimou a probabilidade do resultado. Além disso, o teste de Log-Rank, a Razão de Risco e o teste de Proporcionalidade foram produzidos. Nosso estudo comparou duas coortes: Coorte 1 (71 pacientes - FOLFIRINOX) e Coorte 2 (71 pacientes - gem+nab). Resultados: A análise de risco revelou para a coorte 1 (n= 71 PDAC recebendo FOLFIRINOX) 64,7% de risco de morte. Em relação à coorte 2 (n= 71 PDAC recebendo gem+nab) 66,2% de risco de morte foi evidenciado. RR=0,979 (IC 95% = 0,771 - 1,243, p = 0,860). O metodo de Kaplan-Meier revelou uma probabilidade de sobrevivência no final da janela de tempo de 4,41% vs 12,02%, respectivamente (HR = 0,915 com um IC de 95% de 0,609 - 1376. p = 0,066) O teste Log Rank revelou um X2 = 0,181 (p = 0,670). Conclusão: Apesar do benefício numérico, uma diferença não significativa entre os dois tratamentos de primeira linha atualmente adotados para PDAC metastático (FOLFIRINOX vs Gem + Nab) é relatada.

ABSTRACT (ENG)

Background: Pancreatic cancer (PDAC) represents the 3rd leading cause of cancer death, with increasing incidence of 1% annually and currently the survival profile remains one of the lowest among cancers. During the last decades FOLFIRINOX and Gemcitabine + Nab-paclitaxel represented the standard of care as first line treatment. However a directly comparison among them is scarce in literature. Our trial sought to provide overall survival data comparing these two main chemotherapy schema for metastatic pancreatic cancer using RWD provided by Trinetx. Method: TriNetX is a global federated network of electronic medical

records comprising 127,437,189 patients. Data was retrospectively collected and analyzed for the outcome of death. PSM (propensity score matching) over 11 clinical characteristics were proceeded for cohort balancing. For survival analysis the Kaplan-Meier method estimates the probability of the outcome. Additionally, Log-Rank test, Hazard Ratio and test for proportionality were produced. Our study compared two cohorts: Cohort 1 (71 patients - FOLFIRINOX) and Cohort 2 (71 patients - gem+nab). Results: Risk analysis revealed for cohort 1 (n= 71 PDAC receiving FOLFIRINOX) 64.7% of death risk. In regards of cohort 2 (n= 71 PDAC receiving gem+nab) 66.2% of death risk was reported. RR=0.979 (95% CI = 0.771 - 1.243, p = 0.860). Kaplan - Meier method revealed a survival probability at the end of time window of 4.41% vs 12.02%, respectively (HR = 0.915 with a 95% CI of 0.609 - 1376. p = 0.066) Log Rank Test revealed a X2 = 0.181 (p=0.670). Conclusion: In despite of numerical benefit, a not significant difference between the two currently adopted first line treatment for metastatic PDAC (FOLFIRINOX vs Gem + Nab) is reported.

INTRODUÇÃO / INTRODUCTION

Approximately 64050 new diagnoses of pancreatic cancer are estimated to occur in US during the year of 2023, with 50550 deaths expected this year, ranking as the 3rd leading cause of cancer death among cancers. Additionally, incidence also continued to increase by about 1% annually in both men and women for pancreatic cancer. (Siegel, 2023) In regards of 5-year relative survival rate for all cancers combined, we observed an increase from 49%, during mid-1970s, to 68% for diagnoses from 2012 to 2018. Current survival is highest for cancers of the thyroid (98%), prostate (97%), testis (95%) and remain the lowest for cancers of the pancreas (12%). (SEER 2021; SEER 2022). While neoplasms of the pancreas comprise a broad histopathological spectrum, pancreatic ductal adenocarcinoma (PDAC) is by far the most common type, accounting for about 90% of all pancreas neoplasms (Haeberle L, 2019). Only approximately 20% of patients are suitable for resection when first diagnosed; the remaining 80% are diagnosed with locally advanced pancreatic cancer (LAPC) or metastatic pancreatic cancer (MPC). LAPC is deemed unresectable because direct operation might leave positive resection margins, which jeopardize overall survival (OS) to a degree similar to that in cases not involving resection (Chandrasegaram MD, 2015).

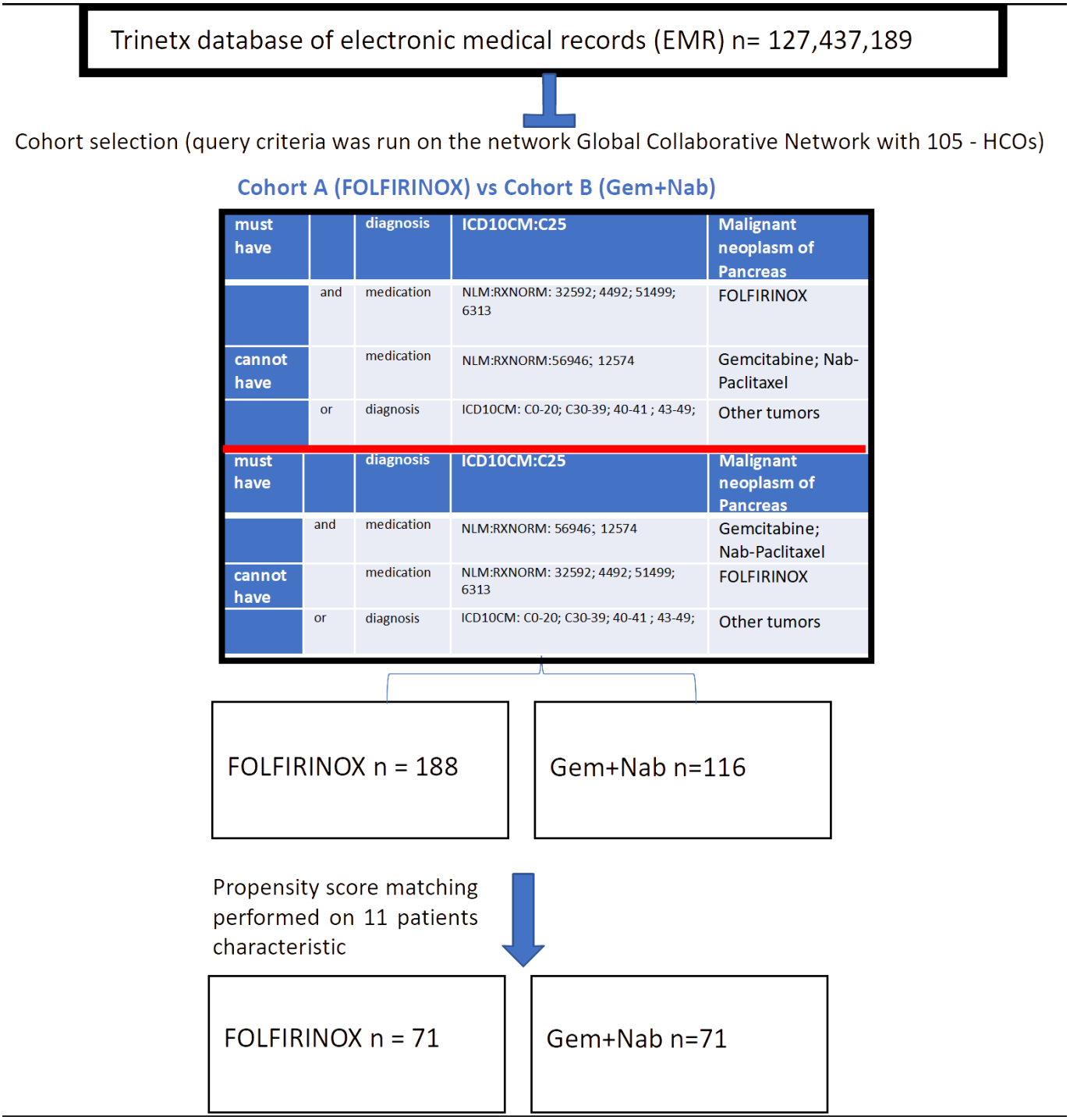
In regards of treatment, recent clinical trials on adjuvant setting established survival benefits of gemcitabine + capecitabine (Neoptolemos JP, 2017) and modified leucovorin (folinic acid), fluorouracil, irinotecan, oxaliplatin (FOLFIRINOX) over gemcitabine monotherapy (Conroy, 2018), remaining the preferred category 1 recommendations for resected PDAC for individuals with high functional status (NCCN, 2023), while gemcitabine (Oettle H, 2013) alone are reserved for individuals with poorer functional status. (Park W, 2021). Negative phase III trial with nab-paclitaxel + gemcitabine failed to change the standard of care for patients with resected pancreatic cancer (Tempero MA, 2023). Metastatic setting shares similar category 1 recommendations, with FOLFIRINOX being the mainstay treatment (Conroy, 2011) until Von Hoff DD and colleagues in 2013 reported in a phase III trial a clinically meaningful improvement in survival of nab-paclitaxel + gemcitabine over gemcitabine alone. New retrospective studies directly comparing FOLFIRINOX and NG reported a longer median OS in the NG group than in the FFX group (11.4 vs 9.6 months; P = 0.002), (Kang J, 2018), However, real world data or phase 3 trials directly comparing FFX vs NG, to date, are not available in literature to our knowledge.

Due to the void of data comparing first line treatment regimens (FFX vs NG) for metastatic PDAC and in an attempt to elucidate this dilemma, real world data acquired from multicentric institutions and compiled into Trinetx software could shed light on how to choose wisely between these 2 currently standard chemotherapy regimens. Our study sought to evaluate RWD through Trinetx software in an attempt to describe the current patterns of treatment among PDAC and its respective impact on overall survival.

METODOLOGIA / METHODS

TriNetX is a global federated network of electronic medical records from 105 healthcare organizations, comprising 127,437,189 patients. Data was retrospectively collected and analyzed for the outcome of death in the time window that started 1 days after the first occurrence of the index event, composed of (1) Malignant neoplasm of pancreas (Histology/Behavior: ADENOCARCINOMA, NOS or DUCT CARCINOMA; with a previously specified staging: Stage 4 disease (based on ICD code) and NIH/NLM RxNorm (for each chemotherapy protocol). PSM (propensity score matching) over 11 clinical characteristics were proceeded for cohort balancing in an attempt to (1) balance covariates, (2) Reduce selection bias and (3) improve casual inference, by matching individuals based on their propensity scores—the probability of receiving the treatment given their covariates described below, ensuring that the distribution of these covariates is similar across groups, controlling for confounding variables that might skew the results. All of the possible confounding factors identified among both cohort characteristics were properly balanced (1 – Age; 2 - Age at index; 3- Race/Ethnicity; 4 – Sex; 5 - Total Billirrubin level; 6 - Albumin level; 7 – INR; 8 - CA 19.9 level; 9 – CEA; 10 - LVEF (cardiac function) ; 11 – BMI). For survival analysis the Kaplan-Meier method estimates the probability of the outcome. Additionally, Log-Rank test, Hazard Ratio and test for Proportionality were produced. Our study was run on the set of 105 HCOs, comparing the outcome of death two cohorts: Cohort A (188 patients) named FOLFIRINOX and Cohort B (116 patients) named gem+nab. The analysis process includes two main steps: 1) Defining the cohorts through query criteria; 2) Setting up and running the analysis. Setting up the analysis required the definition of the index event, outcomes criteria, and the time frame.

Figure 1. Consort 1: Cohort selection method and query terms and criteria.



Cohorts definition - Query Criteria for Cohort 1 (query name: FOLFIRINOX)

This query was run on the network Global Collaborative Network with 105 HCOs, a total of 12 providers responded with patients. The final cohort included 188 patients who matched the query criteria listed in the table below.

Figure 2. Cohorts definition - Query Criteria for Cohort 1 (query name: FOLFIRINOX)

Cohort A				
FOLFIRINOX				
must have		medication	NLM:RXNORM:32592	oxaliplatin
	and	medication	NLM:RXNORM:4492	fluorouracil
	and	medication	NLM:RXNORM:51499	irinotecan
	and	medication	NLM:RXNORM:6313	leucovorin
	and	diagnosis	UMLS:ICD10CM:C25	Malignant neoplasm of pancreas (Histology/Behavior: ADENOCARCINOMA, NOS or DUCT CARCINOMA; Staging: Stage 4)
cannot have		diagnosis	UMLS:ICD10CM:C16	Malignant neoplasm of stomach
	or	diagnosis	UMLS:ICD10CM:C40-C41	Malignant neoplasms of bone and articular cartilage
	or	diagnosis	UMLS:ICD10CM:C43-C44	Melanoma and other malignant neoplasms of skin
	or	diagnosis	UMLS:ICD10CM:C30-C39	Malignant neoplasms of respiratory and intrathoracic organs
	or	diagnosis	UMLS:ICD10CM:C45-C49	Malignant neoplasms of mesothelial and soft tissue
	or all of	diagnosis	UMLS:ICD10CM:C00-C14	Malignant neoplasms of lip, oral cavity and pharynx
		diagnosis	UMLS:ICD10CM:C7A-C7A	Malignant neuroendocrine tumors (C7A)
		diagnosis	UMLS:ICD10CM:D3A-D3A	Benign neuroendocrine tumors (D3A)
	or	diagnosis	UMLS:ICD10CM:D49-D49	Neoplasms of unspecified behavior (D49)
	or	diagnosis	UMLS:ICD10CM:C15	Malignant neoplasm of esophagus
	or	diagnosis	UMLS:ICD10CM:C18	Malignant neoplasm of colon
	or all of	diagnosis	UMLS:ICD10CM:C17	Malignant neoplasm of small intestine
		diagnosis	UMLS:ICD10CM:C19	Malignant neoplasm of rectosigmoid junction
		diagnosis	UMLS:ICD10CM:C20	Malignant neoplasm of rectum
	or	procedure	UMLS:CPT:1007923	Pancreatectomy, proximal subtotal with total duodenectomy
	or all of	medication	NLM:RXNORM:56946	paclitaxel (Brand: Abraxane)
		medication	NLM:RXNORM:12574	gemcitabine

Query Criteria for Cohort 2 (query name: gem+nab)

This query was run on the network Global Collaborative Network with 105 HCOs queried and 105 HCOs responded. A total of 4 providers responded with patients. The final cohort included 116 patients who matched the query criteria listed in the table below.

Figure 3. Query Criteria for Cohort 2 (query name: gem+nab)

Cohort B				
Gam+Nabpaclitaxel				
must have		diagnosis	UMLS:ICD10CM:C25	Malignant neoplasm of pancreas (Histology/Behavior: ADENOCARCINOMA, NOS or DUCT CARCINOMA; Staging: Stage 4)
	and	medication	NLM:RXNORM:12574	gemcitabine
	and	medication	NLM:RXNORM:56946	paclitaxel (Brand: Abraxane)
cannot have		diagnosis	UMLS:ICD10CM:C16	Malignant neoplasm of stomach
	or	diagnosis	UMLS:ICD10CM:C30-C39	Malignant neoplasms of respiratory and intrathoracic organs
	or	procedure	UMLS:CPT:1007923	Pancreatectomy, proximal subtotal with total duodenectomy, partial gastrectomy,
	or	diagnosis	UMLS:ICD10CM:C40-C41	Malignant neoplasms of bone and articular cartilage
	or	diagnosis	UMLS:ICD10CM:C43-C44	Melanoma and other malignant neoplasms of skin
	or	diagnosis	UMLS:ICD10CM:C45-C49	Malignant neoplasms of mesothelial and soft tissue
	or	diagnosis	UMLS:ICD10CM:C00-C14	Malignant neoplasms of lip, oral cavity and pharynx
	or	diagnosis	UMLS:ICD10CM:D3A-D3A	Benign neuroendocrine tumors (D3A)
	or	diagnosis	UMLS:ICD10CM:C7A-C7A	Malignant neuroendocrine tumors (C7A)
	or	diagnosis	UMLS:ICD10CM:D49-D49	Neoplasms of unspecified behavior (D49)
	or	diagnosis	UMLS:ICD10CM:C15	Malignant neoplasm of esophagus
	or	diagnosis	UMLS:ICD10CM:C18	Malignant neoplasm of colon
	or	diagnosis	UMLS:ICD10CM:C20	Malignant neoplasm of rectum
	or	diagnosis	UMLS:ICD10CM:C17	Malignant neoplasm of small intestine
	or	diagnosis	UMLS:ICD10CM:C19	Malignant neoplasm of rectosigmoid junction
	or	medication	NLM:RXNORM:4492	fluorouracil
	or	medication	NLM:RXNORM:51499	irinotecan
	or	medication	NLM:RXNORM:32592	oxaliplatin

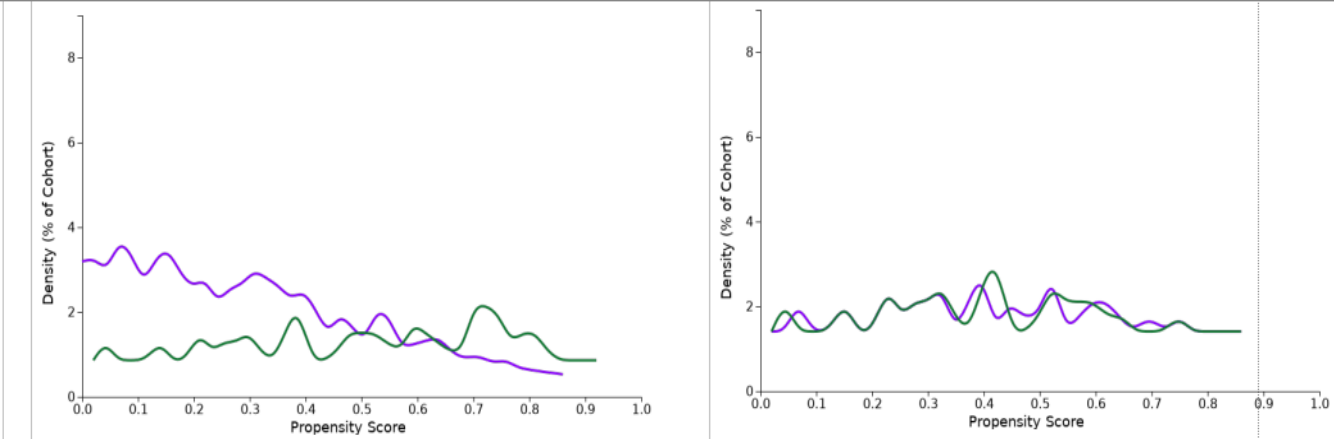
RESULTADOS / RESULTS

Trinetx database comprises a total of 127,437,189 patients that were queried with aforementioned terms. Our analysis initiated with Cohort 1 represented by 188 patients and cohort 2 represented by 116 patients. After propensity score matching our cohort was reduced to Cohort 1 (N = 71) and cohort 2 (N = 71) with balanced aforementioned characteristics.

Figure 4. Cohort 1 and 2 data.

Cohort 1 and cohort 2 patient count before and after propensity score matching		
Cohort	Patient count before matching	Patient count after matching
1 - FOLFIRINOX	188	71
2 - gem+nab	116	71

Propensity score density function - Before and after matching (cohort 1 - purple, cohort 2 - green)



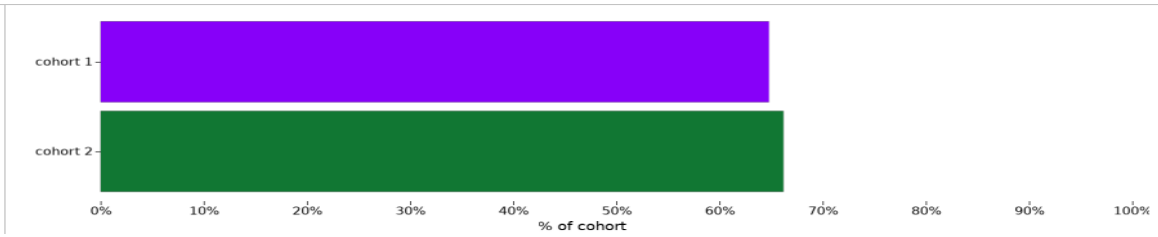
After PSM, risk analysis revealed for cohort 1 (n= 71 PDAC patients that received FOLFIRINOX as first line treatment) 46 reported deaths, representing 64.7% of death risk at the end of the timeline. In regards of cohort 2 (n= 71 PDAC patients that received gem+nab as first line) 47 patients were death, representing 66.2% of death risk at the end of timeline. RR=0.979 (95% CI = 0.771 - 1.243, p = 0.860).

Figure 5. Risk analysis.

Risk analysis

	Cohort	Patients in cohort	Patients with outcome	Risk
1	FOLFIRINOX	71	46	0.648
2	gem+nab	71	47	0.662

		95% CI	z	p
Risk Difference	-0.014	(-0.170, 0.142)	-0.177	0.860
Risk Ratio	0.979	(0.771, 1.243)	N/A	N/A
Odds Ratio	0.940	(0.470, 1.877)	N/A	N/A



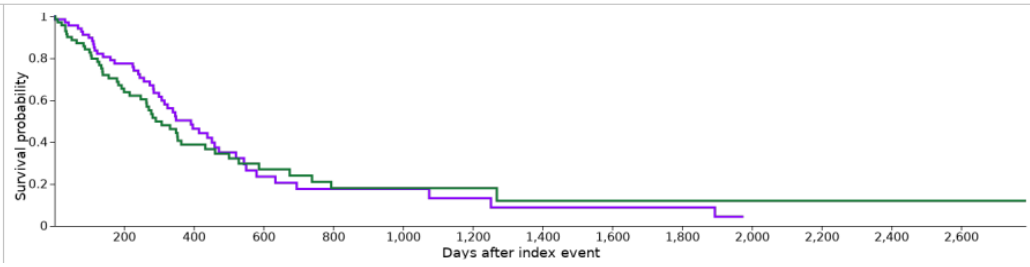
Log rank test and Kaplan - Meier survival analysis were applied in our study data, revealing a median survival of 392 days for cohort 1 and 291 days for cohort 2, with a survival probability at the end of time window of 4.41% vs 12.02%, respectively (HR = 0.915 with a 95% CI of 0.609 - 1376. p = 0.066) Log Rank Test revealed a X2 = 0.181 (p=0.670).

Figure 6. Kaplan-Meier survival analysis.

Kaplan - Meier survival analysis

	Cohort	Patients in cohort	Patients with outcome	Median survival (days)	Survival probability at end of time window
1	FOLFIRINOX	71	46	392	4.41%
2	gem+nab	71	47	291	12.02%
		χ^2	df	p	
Log-Rank Test		0.181	1	0.670	

	Hazard Ratio	95% CI	χ^2	df	p
Hazard Ratio and Proportionality	0.915	(0.609, 1.376)	3.380	1	0.066



DISCUSSÃO / DISCUSSION

Current landscape of PDAC treatment is represented by two pivotal phase 3, RCT's (PRODIGE 4-ACCORD11 trial, Conroy T, 2011; and IMPACT trial, Von Hoff DD, 2013) and in despite of advances acumulated during the last years, patients with locally advanced or metastatic PDAC are generally considered non-curative and managed with palliative intent. FOLFIRINOX was evaluated in the PRODIGE 4-ACCORD11 trial, comparing standard dose gemcitabine to FOLFIRINOX in patients with advanced PDAC. This phase 3, multicenter RCT (randomized controled trial) with n=342 patients revealed a median overall survival (mOS) of 11.1 months vs. 6.8 months favouring FOLFIRINOX. Two years latter, another RCT phase 3 (MPACT) with n=861 patients, randomized to either nab-paclitaxel and gemcitabine (Gem-nabP) or gemcitabine alone. mOS was superior in the Gem-nabP group (8.5 m vs 6.7 m) and PFS of 5.5 vs 3.7 months. However, we still have none RCT, with head-to-head comparison of FOLFIRINOX vs Gem-nabP, and both are considered reasonable first-line treatments for unresectable PDAC. Usually in clinical practice, FOLFIRINOX is generally reserved for fit patients whereas Gem-nabP is preserved for patients with low ECOG or KPS, comorbidities or old age. Additionally, retrospective data revealed that FOLFIRINOX could improve OS, but causes more toxicity in vulnerable population (Raphael MJ, 2021). More recently Napoli-3 Trial (Wainberg ZA, 2023) randomly assigned 770 patients with metastatic PDAC to receive NALIRIFOX (liposomal irinotecan, oxaliplatin, leucovorin, and fluorouracil) versus Gem+Nab. Revealing a mOS of 11.1m (95% CI 10.0-12.1) with NALIRIFOX versus 9.2m (8.3-10.6) with nab-paclitaxel-gemcitabine (HR= 0·83; 95% CI 0·70-0·99; p=0·036), with a similar adverse event profile between arms of treatment. Addittionally, BRAC mutated PDAC patients have some benefit of switch to PARP inhibitor as maintenence therapy, according to POLO trial (Golan T, 2019).

Our study represents an attempt to shed some light in regards of wich first line should be considered a gold standard of care for PDAC and our large and multicenter trial based on EMR databse provided by Trinetx from worlwide healthcare centers is considered to be a positive point. However due to limitations inherent to RWD methodology, our results should be observerd with some caution. Some negative points should be highlighted (1) We were not able to predict the influence of PFS2 over OS analysis, wich could be impacting the final result. (2) BRCA mutational status was not a stratification factor. (3) Cancer specific death was not able to be set as an endpoint. Even with our large database, our results could not lead to a definitive conclusion regarding wich treatment protocol should be adopted as ideal choice. Future trials with novel therapeutics regimens are currently underway in an attempt to improve OS of PDAC, which during the last decades, barely surpass 12 months.

CONCLUSÃO / CONCLUSION

In despite of numerical benefit, here we reported a not significant difference when comparing, head to head, using a real world data from eletronic medical records provided by TrineTx, the two currently adopted as first line treatment for metastatic PDAC (FOLFIRINOX vs Gem + Nab).

Conflict of Interest

The authors declare no conflict of interest.

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REFERÊNCIAS / REFERENCES

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023 Jan;73(1):17-48. doi: 10.3322/caac.21763. PMID: 36633525
2. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER Research Data, 9 Registries (1975-2018), based on the November 2020 submission. National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2021.
3. Surveillance, Epidemio logy, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER Research Data, 17 Registries (2000-2019), based on the November 2021 submission. National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2022.
4. Haeberle L, Esposito I. Pathology of pancreatic cancer. Transl Gastroenterol Hepatol. 2019 Jun 27;4:50.
5. Chandrasegaram MD, Goldstein D, Simes J, Gebski V, Kench JG, Gill AJ. et al. Meta-analysis of radical resection rates and margin assessment in pancreatic cancer. Br J Surg. 2015;102:1459–72.
6. Conroy T, Hammel P, Hebbar M, et al.; Canadian Cancer Trials Group and the Unicancer-GI–PRODIGE Group. FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. N Engl J Med. 2018; 379(25):2395–2406. doi: 10.1056/NEJMoa1809775
7. Oettle H, Neuhaus P, Hochhaus A, et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. JAMA. 2013;310(14):1473–1481
8. Neoptolemos JP, Palmer DH, Ghaneh P, et al. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. Lancet. 2017;389(10073):1011–1024.
9. Park W, Chawla A, O'Reilly EM. Pancreatic Cancer: A Review. JAMA. 2021 Sep 7;326(9):851-862. doi: 10.1001/jama.2021.13027
10. NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. V3.2023
11. Tempero MA, Pelzer U, O'Reilly EM, Winter J, Oh DY, Li CP, Tortora G, Chang HM, Lopez CD, Bekaii-Saab T, Ko AH, Santoro A, Park JO, Noel MS, Frassineti GL, Shan YS, Dean A, Riess H, Van Cutsem E, Berlin J, Philip P, Moore M, Goldstein D, Tabernero J, Li M, Ferrara S, Le Bruchec Y, Zhang G, Lu B, Biankin AV, Reni M; APACT Investigators. Adjuvant nab-Paclitaxel + Gemcitabine in Resected Pancreatic Ductal Adenocarcinoma: Results From a Randomized, Open-Label, Phase III Trial. J Clin Oncol. 2023. Apr 10;41(11):2007-2019
12. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011;364:1817-1825
13. Von Hoff DD, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med. 2013 Oct 31;369(18):1691-703.
14. Kang J, Hwang I, Yoo C, Kim KP, Jeong JH, Chang HM. et al. Nab-paclitaxel plus gemcitabine versus FOLFIRINOX as the first-line chemotherapy for patients with metastatic pancreatic cancer: retrospective analysis. Investigational New Drugs. 2018;36:732–41

15. ©2023 TriNetX, LLC All Rights Reserved. The data used in this study was collected on TriNetX.Avalable at: https://trinetx.com/

16. Raphael MJ, Raskin W, Habbous S, et al. The association of drug-funding reimbursement with survival outcomes and use of new systemic therapies among patients with advanced pancreatic cancer. JAMA Netw Open. 2021;4(11):e2133388–e2133388. doi:10.1001/jamanetworkopen.2021.33388.

17. Wainberg ZA, Melisi D, Macarulla T, Pazo Cid R, Chandana SR, De La Fouchardière C, Dean A, Kiss I, Lee WJ, Goetze TO, Van Cutsem E, Paulson AS, Bekaii-Saab T, Pant S, Hubner RA, Xiao Z, Chen H, Benzaghou F, O'Reilly EM. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023 Oct 7;402(10409):1272-1281. doi: 10.1016/S0140-6736(23)01366-1.

18. Golan T, Hammel P, Reni M, et al. Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. N Engl J Med. 2019;381(4):317–327. doi:10.1056/NEJMoa1903387.