2025 ASCO® ANNUAL MEETING

PANOVA-3: Phase 3 study of Tumor Treating Fields (TTFields) with gemcitabine and nab-paclitaxel (GnP) for locally advanced pancreatic adenocarcinoma (LA-PAC)

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Key Takeaway Points/Conclusions

PANOVA-3 is the first phase 3 trial in patients with unresectable LA-PAC to show an OS benefit over gemcitabine/nab-paclitaxel

Survival benefit for patients is supported by significantly improved QoL and pain-free survival* compared with GnP alone

The only frequently reported TTFields toxicity was localized skin reactions

PANOVA-3 establishes TTFields with GnP as a potential new standard paradigm for unresectable LA-PAC

*as the time to a ≥ 20-point increase from baseline on a patient-reported visual analogue scale for pain or death.
GnP, gemcitabine/nab-paclitaxel; LA-PAC, locally advanced pancreatic adenocarcinoma; OS, overall survival; TTFields, Tumor Treating Fields.

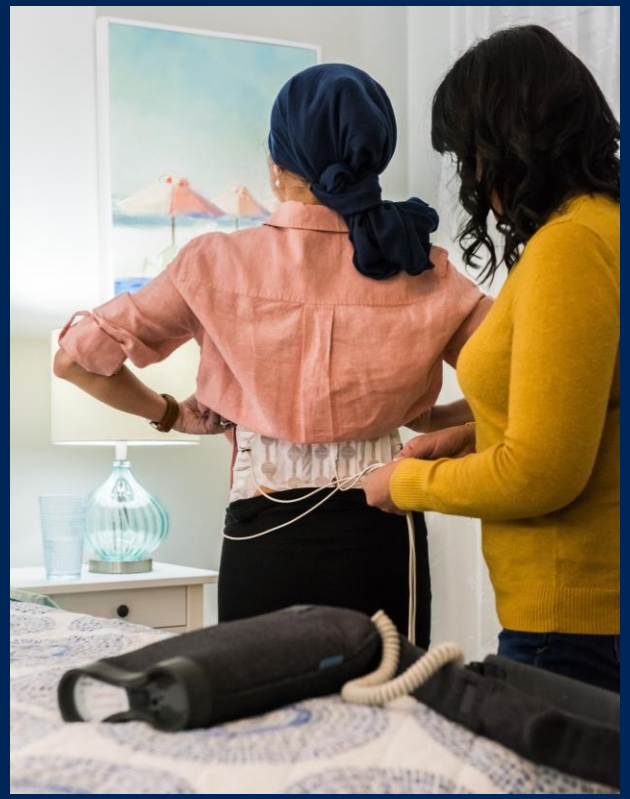
LA- PAC, a high unmet need

- Pancreatic adenocarcinoma remains a high unmet need with a modest 5-year survival rate of 8%[1,2]
  - About 30–35% of patients present with LA-PAC* and only 10–15% of them will be eligible for potentially curative surgery[3]
  - The remaining patients are incurable and will experience debilitating symptoms, especially pain
- The current SOC for unresectable LA-PAC is chemotherapy (GnP, FOLFIRINOX, NALIRIFOX) ± radiation[4-6]
- While most trials of novel agents have focused on patients with metastatic disease,[7-9] **recent studies in patients with LA-PAC have failed** to demonstrate overall survival benefit over the current SOC[10,11]

*LA-PAC was defined as histological/cytological diagnosis of *de novo* adenocarcinoma of the pancreas, which was deemed unresectable, locally advanced by investigator.
GnP, gemcitabine/nab-paclitaxel; FOLFIRINOX, 5-FU/leucovorin, irinotecan, and oxaliplatin; LA-PAC, locally advanced pancreatic adenocarcinoma; NALFIRINOX, liposomal irinotecan, oxaliplatin, 5-FU/leucovorin, SOC, standard of care; References: 1. National Cancer Institute 2025; 2. American Cancer Society. Cancer Facts & Figures 2025. 3. Park W, et al. JAMA. 2021;326(9):851-862; 4. Conroy T, et al. Ann Oncol 2023;34(11):987-1002; 5. National Comprehensive Cancer Network (NCCN). NCC Guidelines in Oncology. Pancreatic Adenocarcinoma. 2024; 6. Wainberg ZA, et al. Lancet 2023 Oct 7;402(10409):1272-1281; 7. Picozzi VJ, et al. J Clin Oncol 43, 2025 (suppl 4; abstr 673); 8. Hu ZI, et al. Nat Rev Gastroenterol Hepatol 2024; 21 (1):7-24; 1961-703; 9. Anderson EM, et al. Cancers (Basel)2021; 13(21):5510; 10. De La Fouchardiere C, et al. J Clin Oncol 2024;42(9):105-66; 7); 11. Hammel P et al. JAMA 2016;315(17):1844-53.

TTFields therapy

- TTFields are electric fields that disrupt processes critical for cancer cell division[1-3] and may trigger an enhanced antitumor immune response
- TTFields therapy is delivered noninvasively to the tumor site via a portable device that consists of a field generator and arrays placed on the skin[4,5]
- TTFields concomitant with systemic therapy is approved in the US and Europe for GBM, MPM, and metastatic NSCLC,[6,7] and in Japan for GBM
- TTFields with gemcitabine ± nab-paclitaxel was feasible and well tolerated in patients with advanced pancreatic adenocarcinoma in the phase 2 PANOVA pilot trial[8]

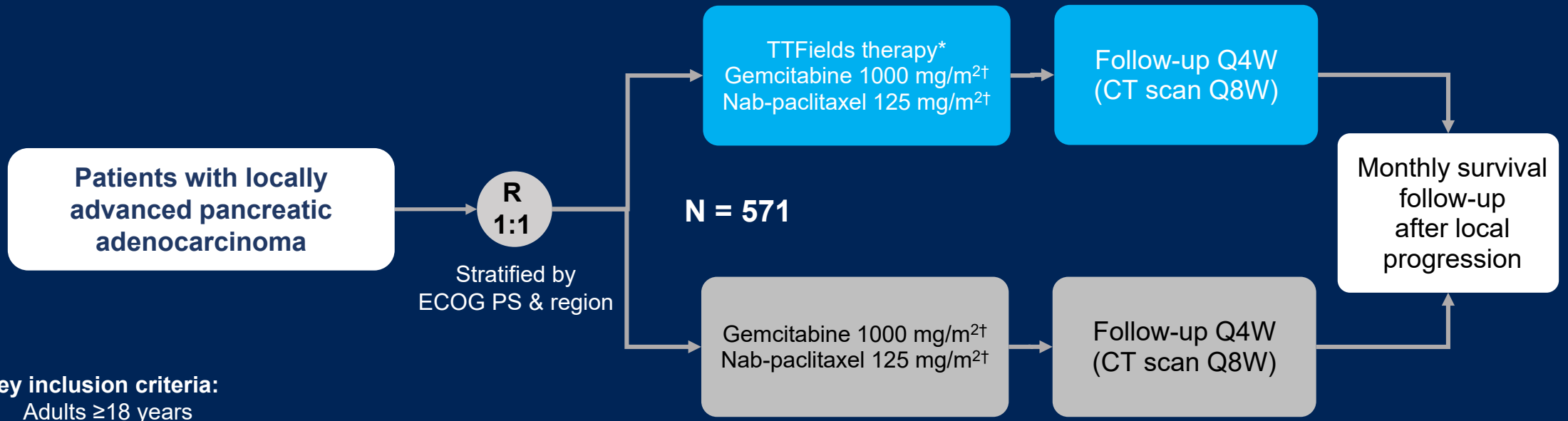


Actor portrayal

GBM, glioblastoma; MPM, malignant pleural mesothelioma; NSCLC, non-small cell lung cancer; TTFields, Tumor Treating Fields.

1. Kirson ED et al. Cancer Res. 2004;64(9):3288-3295. 2. Mun EJ et al. Clin Cancer Res. 2018;24(2):266-275. 3. Voloshin T et al. Cancers (Basel). 2020;12(10):3016; 4. Optune. Instructions for Use. Novocure; January 2019. 5. NovoTTF-100L. Instructions for Use for Unresectable Malignant Pleural Mesothelioma. Novocure; 2021; 6. Optune Lua® for Non-Small Cell Lung Cancer (NSCLC) – Patient Information and Operation Manual. Available at: https://assets.novocure.biz/optunelua/2024-10/Optune%20Lua%20NSCLC%20ITE%20PIOM_v%2008.pdf; 7. Optune Gio®– Instructions for Use. Available at: https://www.optunegio.com/instructions-for-use; 8. Rivera F et al. Pancreatology 2017; 19(1):64-72.

PANOVA-3 study design



Key inclusion criteria:
- Adults ≥18 years
- Previously untreated, biopsy confirmed disease
- Life expectancy ≥3 months
- ECOG PS 0-2

Key exclusion criteria:
- Prior palliative treatment to the tumor
- Implanted electronic medical device in torso
- Known allergies to medical adhesives, hydrogel or chemotherapies

Study sites: 198 across 20 countries (North and South America, Europe, Asia)‡
Enrollment: March 2018 – March 2023

Data cut-off: October 16, 2024
Registration number: NCT03377491

*150 kHz, 18h/day; †On days 1, 8, and 15 of each 28-day cycle; ‡ US, Mexico, Brazil, Canada; Spain, Hungary, Czech Republic, France, Poland, Germany, Austria, Switzerland, Italy, Israel, Belgium, Croatia; China, South Korea, Australia and Hong Kong;
CT, computer tomography; ECOG PS, Eastern Cooperative Oncology Group Performance Status; R, randomization; TTFields, Tumor Treating Fields; Q4W, every 4 weeks; Q8W, every 8 weeks.

PANOVA-3: Endpoints and statistical analyses

Primary endpoint

- OS

Secondary endpoints (selected)

- PFS (powered secondary endpoint)
- Local PFS
- Pain-free survival
- 1-yr survival rate*
- ORR †
- Safety

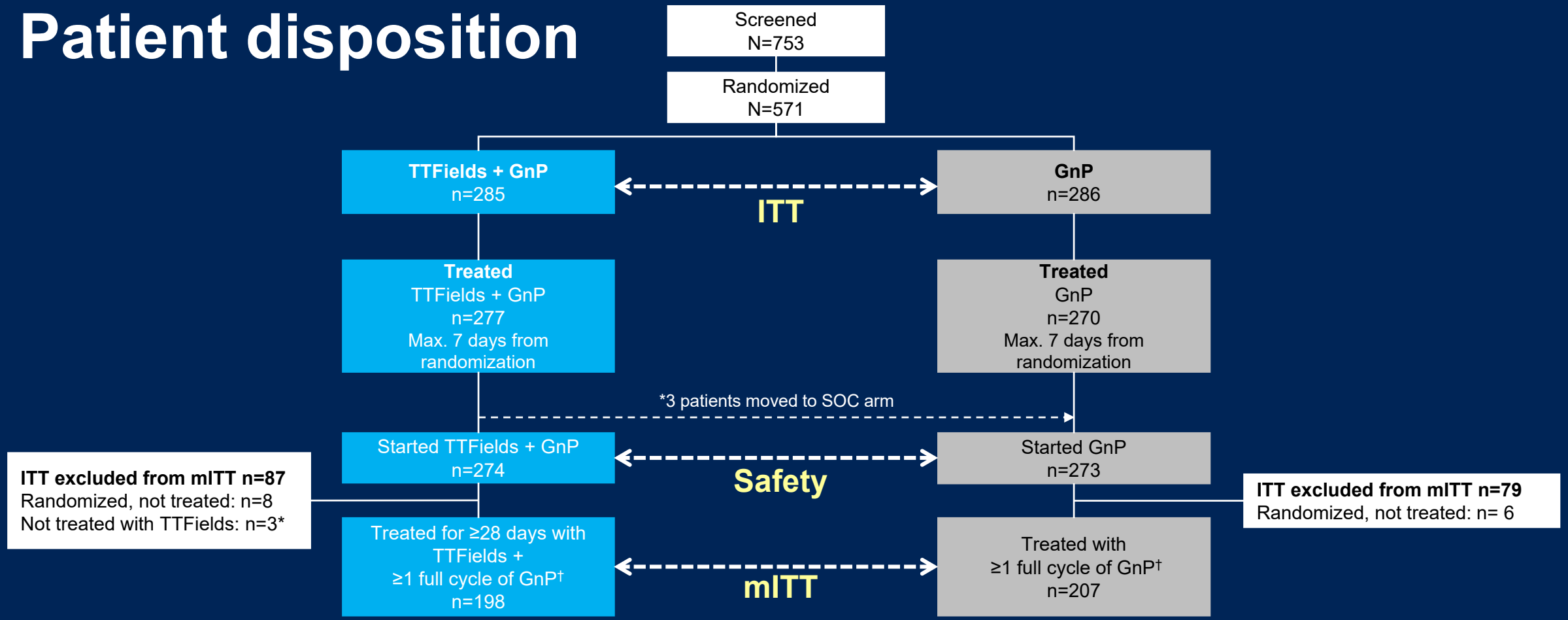
Post-hoc analysis

- Distant PFS

- Primary and secondary endpoints were investigated in the ITT and mITT populations (= all patients treated with ≥1 full cycle of GnP and/or ≥28 days with TTFields)
- OS was analyzed using the KM method, comparison of KM curves was done using two-sided log-rank test stratified by region
- Pain-free survival: time from randomization until ≥20-point increase from baseline in a patient-reported visual analogue scale for pain or death

*Compared using one-sided t-test after the directionality of the effect was established; †Compared using one-sided Fisher's exact test with α=0.05.
GnP, gemcitabine/nab-paclitaxel; ITT, intent-to-treat population; KM, Kaplan-Meier; mITT, modified intent-to-treat population; ORR, overall response rate; OS, overall survival; PFS, progression-free survival, TTFields, Tumor Treating Fields.

Patient disposition



- ITT included all randomized patients regardless of treatment received; mITT included all patients who received at least one complete cycle of treatment (≥28 days with TTFields + ≥1 full cycle of GnP)
- The number of discontinuations in both arms during the first 28 days after inclusion was mostly related to disease progression or patients' decision

† One full GnP cycle is defined as 3 complete administrations per cycle.
GnP, gemcitabine/nab-paclitaxel; ITT, intent-to-treat population; mITT, modified intent-to-treat population; TTFields, Tumor Treating Fields..

PANOVA-3: Patients characteristics

- Characteristics were generally well balanced between the 2 study arms
  - More females than males in the gemcitabine/ nab-paclitaxel arm
- High CA 19-9 values may be indicative of very advanced disease

		TTFields + GnP (n=285)	GnP (n=286)	Overall (n=571)
Median age (range)	Years	67 (31, 90)	67.5 (40, 88)	67 (31, 90)
Gender, n (%)	Male	147 (51.6)	125 (43.7)	272 (47.6)
	Female	138 (48.4)	161 (56.3)	299 (52.4)
Race, n (%)	American Indian or Alaska Native	9 (3.2)	4 (1.4)	13 (2.3)
	Asian	44 (15.4)	44 (15.4)	88 (15.4)
	Black or African American	16 (5.6)	14 (4.9)	30 (5.3)
	White	202 (70.9)	204 (71.3)	406 (71.1)
	Other	3 (1.1)	5 (1.7)	8 (1.4)
	Not Reported	11 (3.9)	15 (5.2)	26 (4.6)
ECOG PS, n (%)	0	109 (38.2)	111 (38.8)	220 (38.5)
	1	166 (58.2)	163 (57.0)	329 (57.6)
	2	10 (3.5)	12 (4.2)	22 (3.9)
CA 19-9, n (%)	Normal (≤37 U/mL)	48 (16.8)	44 (15.4)	92 (16.1)
	Elevated (38–1,000 U/mL)	140 (49.1)	152 (53.1)	292 (51.1)
	High (>1,000 U/mL)	88 (30.9)	79 (27.6)	167 (29.2)
	Untested	9 (3.2)	11 (3.8)	20 (3.5)

CA19-9, carbohydrate antigen 19-9; ECOG PS, Eastern Cooperation Oncology Group performance status; GnP, gemcitabine/nab-paclitaxel; TTFields, Tumor Treating Fields.

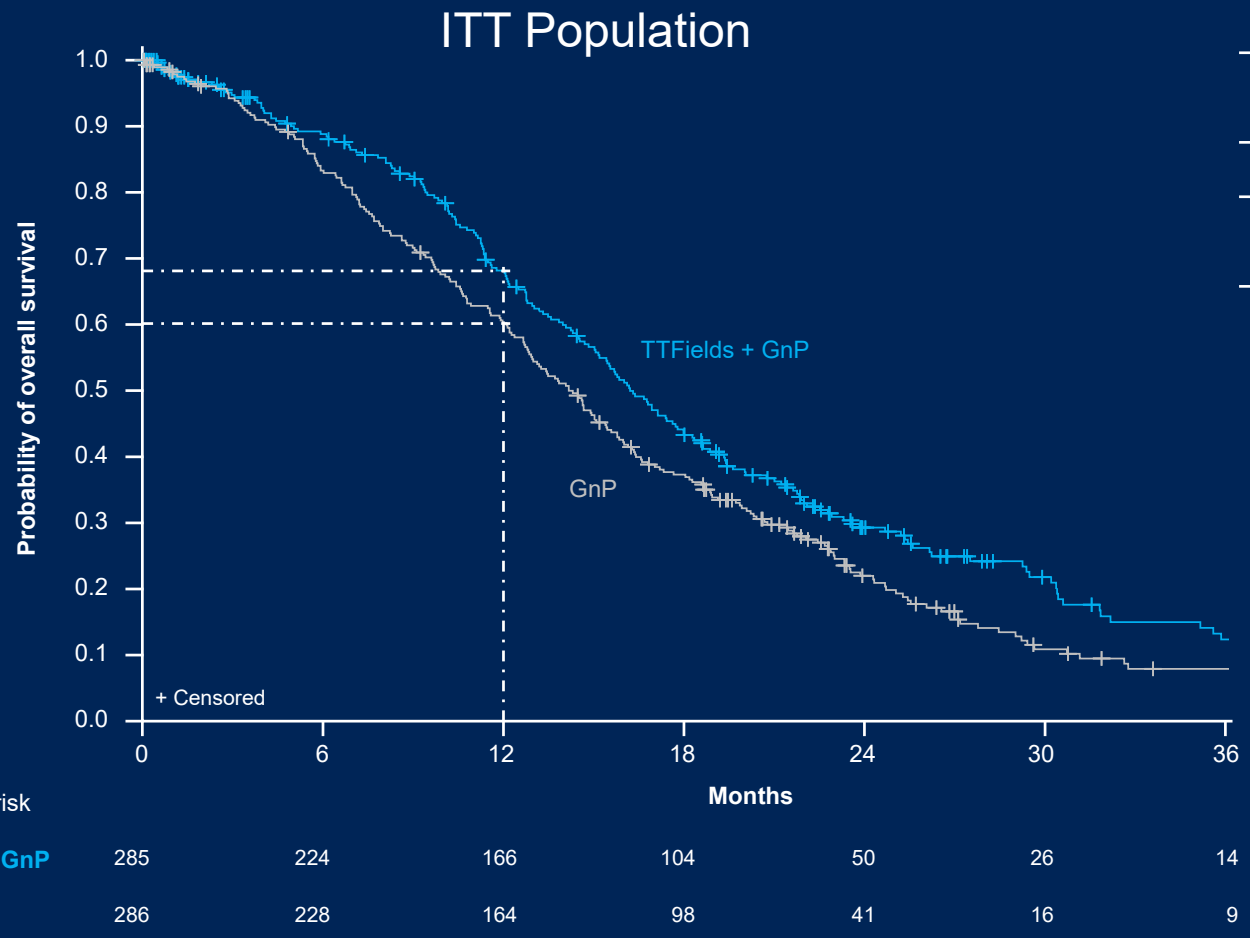
PANOVA-3: Treatment characteristics

- Duration of exposure to gemcitabine and nab-paclitaxel was similar in the study arms
- The distribution of salvage therapies was balanced between the study arms

Duration of exposure – ITT population	TTFields + GnP (n=285)	GnP (n=286)
Gemcitabine		
Median cycles received, n (range)	6.0 (1.0, 57.0)	6.0 (1.0, 30.0)
Median duration of exposure, weeks (range)	24.1 (0.1, 232.4)	22.1 (0.1, 134.1)
Nab-paclitaxel		
Median cycles received, n (range)	6.0 (1.0, 57.0)	5.0 (1.0, 30.0)
Median duration of exposure, weeks (range)	23.0 (0.1, 232.4)	21.4 (0.1, 134.1)
TTFields		
Median daily device usage, % (range)	62.1 (0, 99.0)	NA
Median duration of exposure, weeks (range)	27.6 (0.1, 234.4)	NA
Median follow-up, months (range)	13.5 (0.03, 55.2)	12.9 (0.03, 50.1)

GnP, gemcitabine/nab-paclitaxel; NA, not applicable; TTFields, Tumor Treating Fields.

Primary endpoint: overall survival



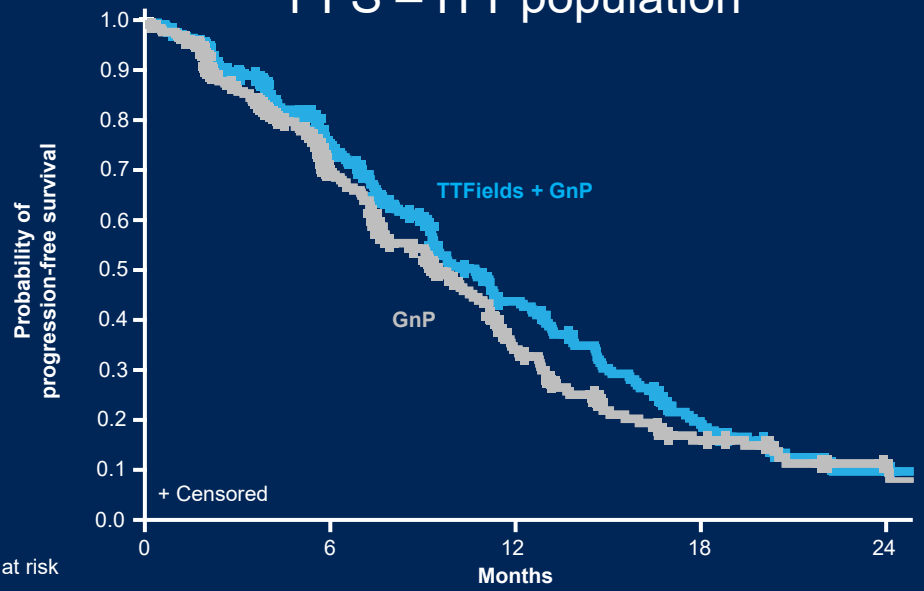
ITT	TTFields + GnP	GnP	P-value
Median OS (95% CI) **Events**	16.2 (15.0, 18.0) 201	14.2 (12.8, 15.4) 230	**0.039**
	HR = 0.82 (95% CI: 0.68, 0.99)		
1-year survival rate, Median (95% CI)	68.1 (62.0, 73.5)	60.2 (54.2, 65.7)	**0.029**

mITT	TTFields + GnP	GnP	P-value
Median OS (95% CI) **Events**	18.3 (16.1, 20.0) 151	15.1 (13.4, 17.0) 169	**0.023**
	HR = 0.77 (95% CI: 0.62, 0.97)		
1-year survival rate, Median (95% CI)	75.1 (68.3, 80.6)	65.9 (59.0, 72.0)	**0.022**

CI, confidence interval; GnP, gemcitabine/nab-paclitaxel; HR, hazard ratio; ITT, intent-to-treat population; mITT, modified intent-to-treat population; OS, overall survival; TTFields, Tumor Treating Fields.

Secondary endpoints: PFS and local PFS

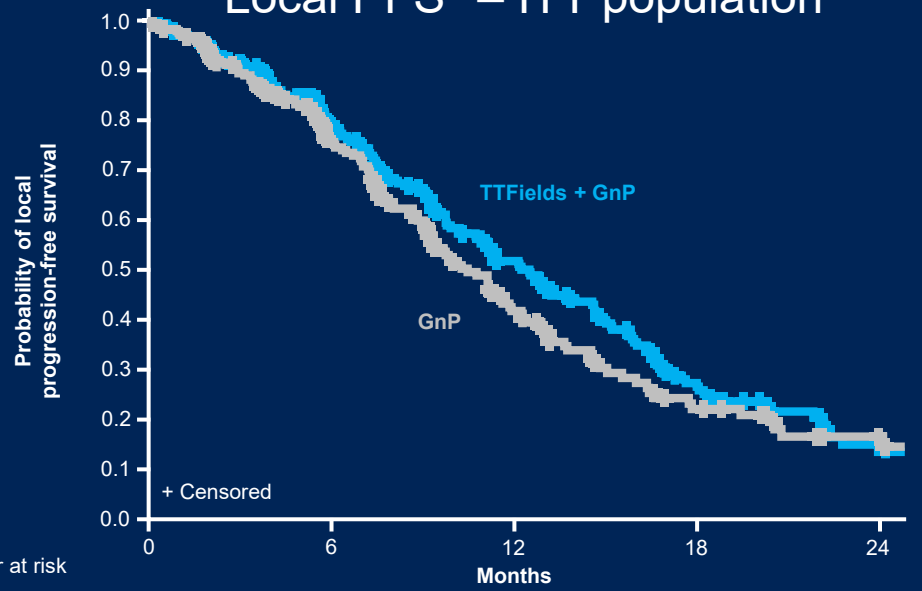
PFS – ITT population



Number at risk					
TTFields + GnP	285	153	79	30	9
GnP	286	133	50	17	6

	TTFields + GnP	GnP	P-value
Median PFS (95% CI) **Events**	10.6 (9.2, 12.2) 176	9.3 (7.6, 11.1) 162	**0.137**
HR = 0.85 (95% CI: 0.68, 1.05)			
1-year PFS rate, Median (95% CI)	43.9 (36.9, 50.6)	34.1 (27.1, 41.2)	**0.026**

Local PFS* – ITT population

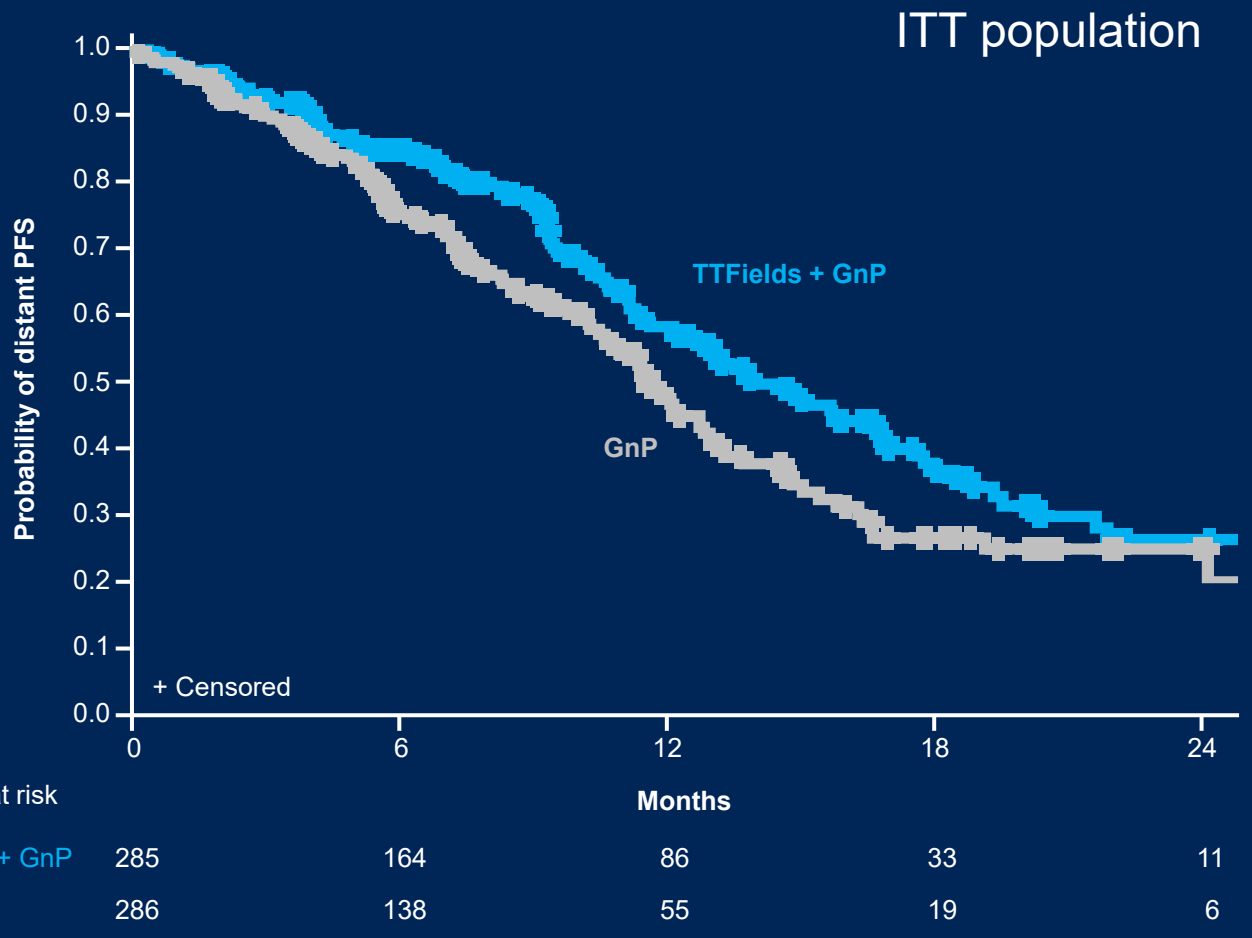


Number at risk					
TTFields + GnP	285	162	90	36	9
GnP	286	139	56	20	8

	TTFields + GnP	GnP	P-value
Median local PFS (95% CI) **Events**	12.5 (10.7, 14.5) 155	10.4 (9.1, 11.8) 139	**0.151**
HR = 0.84 (95% CI: 0.67, 1.06)			
1-year local PFS rate, Median (95% CI)	51.9 (44.8, 58.6)	41.8 (34.2, 49.2)	**0.027**

*Progressive disease per revised RECIST version 1.1 in the absence of distant metastasis, including non-regional lymph node metastasis, and abdominal metastases.
CI, confidence interval; GnP, gemcitabine/nab-paclitaxel; HR, hazard ratio; ITT, intent-to-treat population; PFS, progression-free survival; TTFields, Tumor Treating Fields.

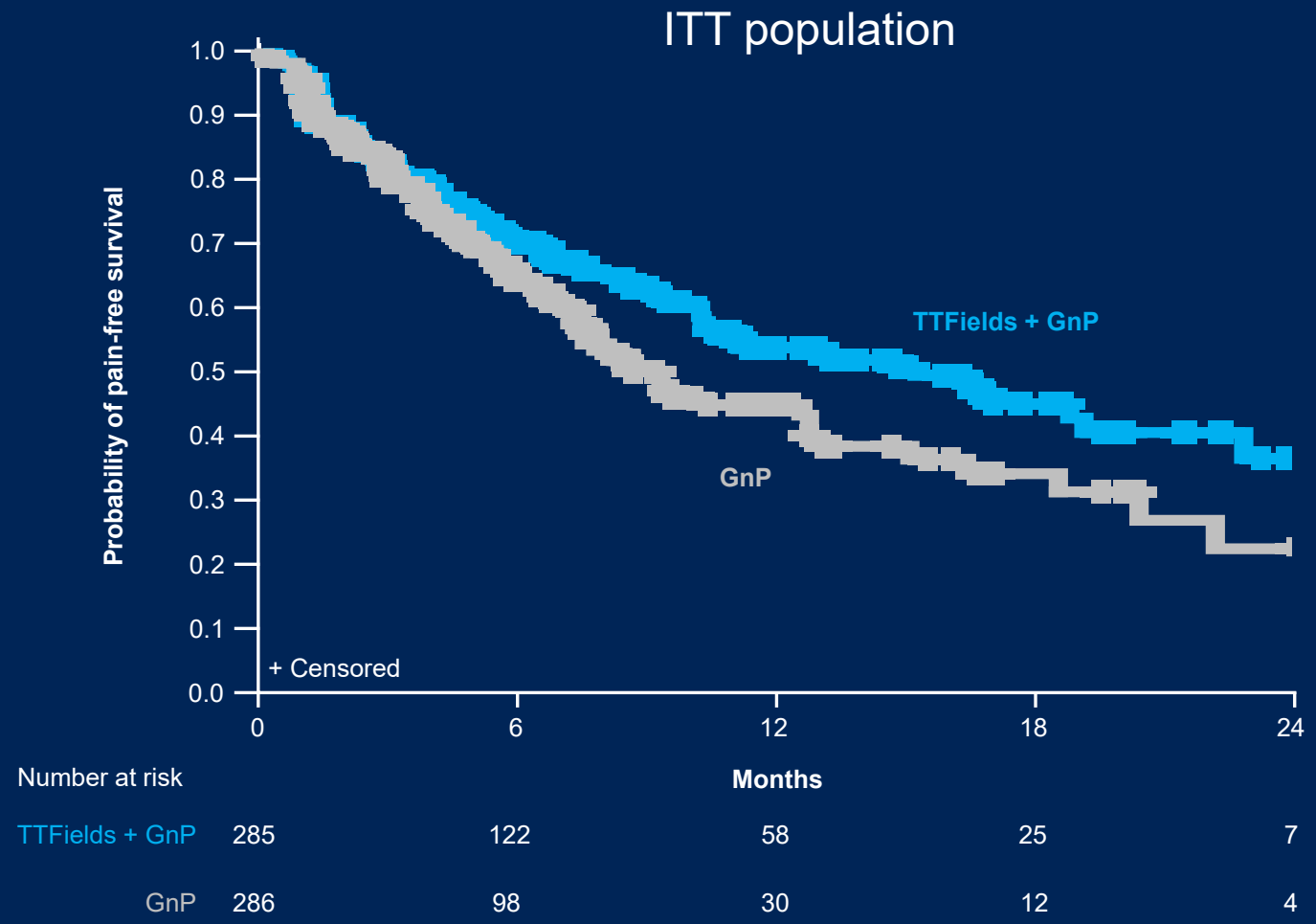
Post-hoc analysis: Distant PFS*



ITT	TTFields + GnP	GnP	P-value
Median distant PFS (95% CI)	13.9 (12.2, 16.8)	11.5 (10.4, 12.9)	**0.022**
Events	113	119	
	HR = 0.74 (95% CI: 0.57, 0.96)		
1-year distant PFS rate, Median (95% CI)	58.5 (50.7, 65.4)	47.6 (39.6, 55.2)	**0.024**

*Defined as progressive disease per revised RECIST version 1.1 in the absence of local progression.
CI, confidence interval; GnP, gemcitabine/nab-paclitaxel; HR, hazard ratio; ITT, intent-to-treat population; PFS, progression-free survival; TTFields, Tumor Treating Fields.

Secondary endpoint: pain-free survival*

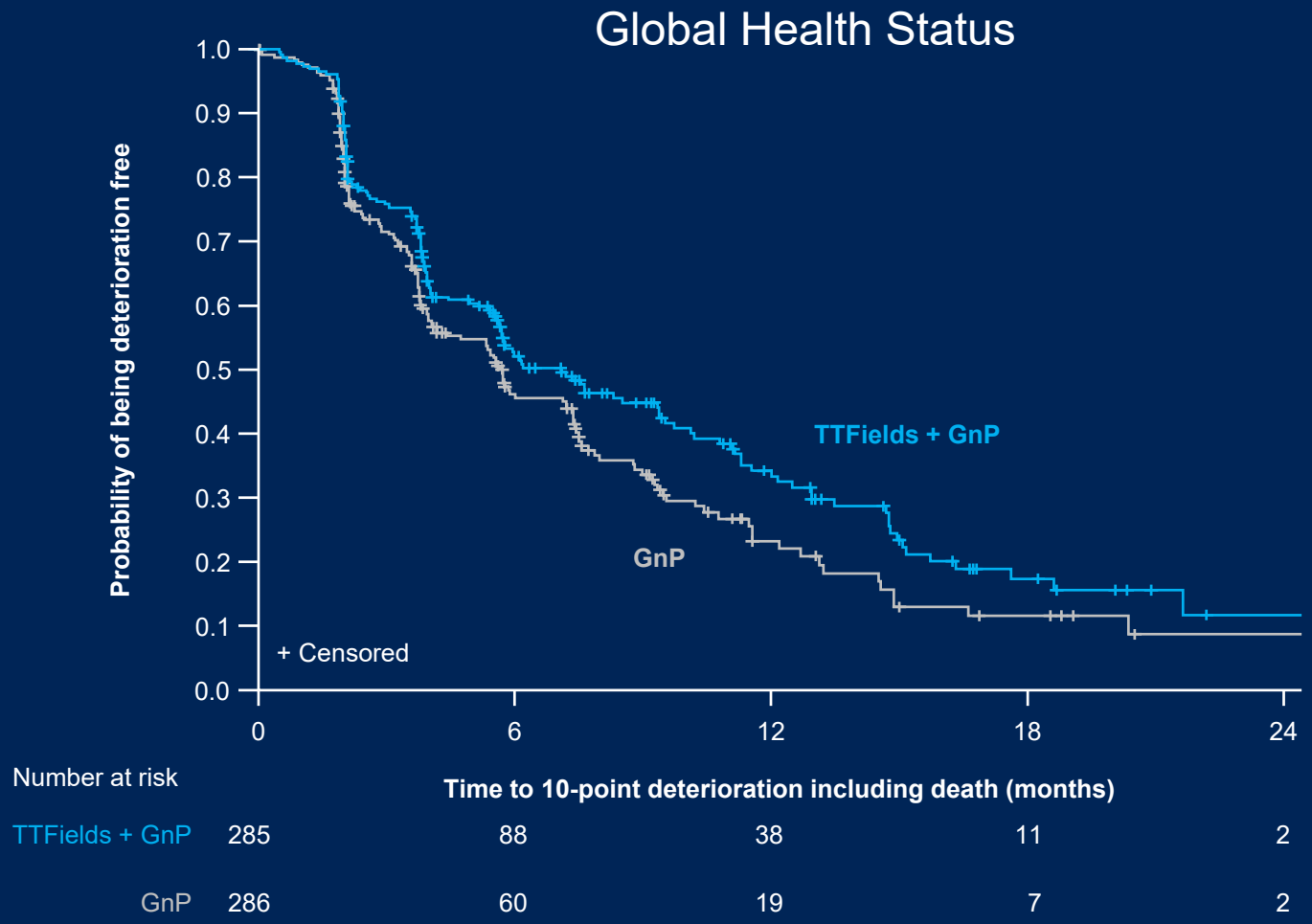


ITT	TTFields + GnP	GnP	P-value
Median pain-free survival (95% CI)	15.2 (10.3, 22.8)	9.1 (7.4, 12.7)	**0.027**
Events	102	110	
	HR = 0.74 (95% CI: 0.56, 0.97)		
1-year pain-free survival rate, Median (95% CI)	54.1 (46.2, 61.3)	45.1 (36.8, 53.0)	**0.056**

*Pain-free survival was defined as the time to a ≥ 20-point increase **from baseline o**n a patient-reported visual analogue scale (VAS) for pain or death

CI, confidence interval; GnP, gemcitabine/nab-paclitaxel; HR, hazard ratio; ITT, intent-to-treat population; TTFields, Tumor Treating Fields; VAS, visual analogue scale.

Secondary endpoint: Quality of Life



- QoL analyses were performed in all patients using the EORTC QLQ C30 questionnaire with the pancreatic cancer-specific PAN26 addendum
- Deterioration-free survival in global health status, pain and digestive problems were significantly improved in patients receiving TTFields Therapy
- Full QoL data will be presented in the near future

ITT	TTFields + GnP	GnP	P-value
Median time to deterioration* (95% CI)	7.1 (5.7, 9.4)	5.7 (4.1, 7.4)	**0.023**
Events	146	160	
	HR = 0.77 (95% CI: 0.61, 0.97)		
1-year deterioration-free rate, median (95% CI)	33.3 (26.1, 40.8)	23.3 (16.6, 30.7)	**0.0414**

*Defined as the first time-point a patient experienced a deterioration of ≥10 points in the respective QoL scale or death.
GnP, gemcitabine/nab-paclitaxel; QoL, quality of life; TTFields; Tumor Treating Fields.

Safety summary

AEs occurring in ≥20% of patients overall, n (%)	TTFields + GnP (N=274)		GnP (N=273)	
	All grades	Grade ≥3	All grades	Grade ≥3
Any AE	268 (97.8)	243 (88.7)	270 (89.9)	230 (84.2)
Neutropenia	172 (62.8)	131 (47.8)	180 (65.9)	130 (47.6)
Fatigue	165 (60.2)	29 (10.6)	148 (54.2)	21 (7.7)
Anemia	161 (58.8)	60 (21.9)	158 (57.9)	61 (22.3)
Thrombocytopenia	122 (44.5)	39 (14.2)	133 (48.7)	32 (11.7)
Diarrhea	119 (43.4)	11 (4.0)	125 (45.8)	15 (5.5)
Neuropathy peripheral	112 (40.9)	20 (7.3)	81 (29.7)	18 (6.6)
Nausea	107 (39.1)	11 (4.0)	121 (44.3)	7 (2.6)
Edema peripheral	107 (39.1)	5 (1.8)	99 (36.3)	2 (0.7)
Leukopenia	85 (31.0)	47 (17.2)	98 (35.9)	42 (15.4)
Dermatitis	**82 (29.9)**	**8 (2.9)**	**8 (2.9)**	**0**
Vomiting	82 (29.9)	7 (2.6)	79 (28.9)	15 (5.5)
Hepatic enzyme increased	75 (27.4)	35 (12.8)	72 (26.4)	24 (8.8)
Pyrexia	74 (27.0)	6 (2.2)	64 (23.4)	2 (0.7)
Abdominal pain	73 (26.6)	11 (4.0)	83 (30.4)	12 (4.4)
Rash	**71 (25.9)**	**5 (1.8)**	**23 (8.4)**	**1 (0.4)**
Alopecia	71 (25.9)	0	86 (31.5)	2 (0.7)
Musculoskeletal pain	70 (25.5)	3 (1.3)	79 (28.9)	5 (1.8)
Constipation	65 (23.7)	1 (0.4)	57 (20.9)	0
Hypokalemia	63 (23.0)	12 (4.4)	70 (25.6)	20 (7.3)
Pruritus	**61 (22.3)**	**0**	**23 (8.4)**	**0**

AE, n (%)	TTFields + GnP (N=274)		GnP (N=273)	
	All grades	Grade ≥3	All grades	Grade ≥3
Serious AE	147 (53.6)	143 (52.2)	131 (48.0)	130 (47.6)
AE leading to device discontinuation	23 (8.4)		NA	
AE leading to chemotherapy discontinuation	47 (17.2)		43 (15.8)	
AE leading to death	17 (6.2)		16 (5.9)	

- Rates of AEs were similar between arms
- Toxicity profile as expected for treatment with gemcitabine/nab-paclitaxel overall[1]
- Higher number of skin AEs seen in the TTFields arm

AE, adverse event; GnP, gemcitabine/nab-paclitaxel; TTFields, Tumor Treating Fields.

1. Von Hoff DD, et al. NEJM 2013;369(18):1691-703.

Device-related adverse events

- No new safety signals were observed
- No deaths were attributed to TTFields
- Skin AEs were the most common device-related AEs
  - Majority were grade 1/2 and manageable with appropriate skin-care routines
  - 7.7% of patients reported a grade 3 skin AE

Device-related AEs, n (%)	TTFields + GnP (N=274)	
	All grades	Grade ≥3
Any AE	222 (81.0)	26 (9.5)
Any serious AE	1 (0.4)	0
Any AE leading to TTFields discontinuation	23 (8.4)	7 (2.6)
Any AE leading to death	0	0
AEs occurring in ≥2% of patients		
Dermatitis	76 (27.7)	8 (2.9)
Rash	48 (17.5)	4 (1.5)
Pruritus	41 (15.0)	0
Rash maculo-papular	33 (12.0)	3 (1.1)
Erythema	29 (10.6)	0
Skin irritation	25 (9.1)	2 (0.7)
Skin reaction	17 (6.2)	1 (0.4)
Skin ulcer	14 (5.1)	1 (0.4)
Blister	10 (3.6)	0
Fatigue	12 (4.4)	2 (0.7)
Abdominal pain	9 (3.3)	0
Diarrhea	7 (2.6)	0
Skin injury	8 (2.9)	0
Thermal burn	6 (2.2)	0

AE, adverse event; GnP, gemcitabine/nab-paclitaxel; TTFields, Tumor Treating Fields.

Key Takeaway Points/Conclusions

PANOVA-3 is the first phase 3 trial in patients with unresectable LA-PAC to show an OS benefit over gemcitabine/nab-paclitaxel

Survival benefit for patients is supported by significantly improved QoL and pain-free survival* compared with GnP alone

The only frequently reported TTFields toxicity was localized skin reactions

PANOVA-3 establishes TTFields with GnP as a potential new standard paradigm for unresectable LA-PAC

*as the time to a ≥ 20-point increase from baseline on a patient-reported visual analogue scale for pain or death.
GnP, gemcitabine/nab-paclitaxel; LA-PAC, locally advanced pancreatic adenocarcinoma; OS, overall survival; TTFields, Tumor Treating Fields.

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Tumor Treating Fields With Gemcitabine and Nab-Paclitaxel for Locally Advanced Pancreatic Adenocarcinoma: Randomized, Open-Label, Pivotal Phase III PANOVA-3 Study

Original Reports | Gastrointestinal Cancer

Tumor Treating Fields With Gemcitabine and Nab-Paclitaxel for Locally Advanced Pancreatic Adenocarcinoma: Randomized, Open-Label, Pivotal Phase III PANOVA-3 Study

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ABSTRACT

PURPOSE Tumor treating fields (TTFields) use alternating electric fields to disrupt cancer cell proliferation. Feasibility of TTFields therapy with gemcitabine/nab-paclitaxel was previously demonstrated in patients with advanced pancreatic adenocarcinoma. PANOVA-3 was designed to confirm safety and efficacy of TTFields in patients with unresectable locally advanced pancreatic adenocarcinoma (LA-PAC).

METHODS In this global phase III trial, 571 patients with newly diagnosed LA-PAC were randomly assigned to receive gemcitabine 1,000 mg/m² and nab-paclitaxel 125 mg/m² on days 1, 8, and 15 of a 28-day cycle with or without TTFields. The primary end point was overall survival (OS). Secondary end points included progression-free survival (PFS), local PFS, pain-free survival, and overall response rate (ORR). Distant PFS was analyzed post hoc.

RESULTS OS was significantly prolonged using TTFields with gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel (median, 16.2 months [95% CI, 15.0 to 18.0] *v* 14.2 months [95% CI, 12.8 to 15.4]; hazard ratio [HR], 0.82 [95% CI, 0.68 to 0.99]; *P* = .039). PFS, local PFS, and ORR were not improved. Pain-free survival was significantly prolonged with TTFields with gemcitabine/nab-paclitaxel (median, 15.2 months [95% CI, 10.3 to 22.8] *v* 9.1 months [95% CI, 7.4 to 12.7]; HR, 0.74 [95% CI, 0.56 to 0.97]; *P* = .027), as was distant PFS (median, 13.9 months [95% CI, 12.2 to 16.8] *v* 11.5 months [95% CI, 10.4 to 12.9]; HR, 0.74 [95% CI, 0.57 to 0.96]; *P* = .022). Device-related skin adverse events (AEs) were experienced by 76.3% of patients. Most device-related skin AEs were mild to moderate, with 7.7% of patients reporting a grade 3 AE.

CONCLUSION This study demonstrated significant OS, pain-free survival, and distant PFS benefits for TTFields with gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel in patients with unresectable LA-PAC, with no additive systemic toxicity.

ACCOMPANYING CONTENT

Appendix
Data Sharing Statement
Data Supplement
Protocol

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INTRODUCTION

Most patients with pancreatic adenocarcinoma present with advanced disease at diagnosis,[1] which remains difficult to treat. With 5-year survival rates between 8% and 13%,[1,2] prognosis for patients with pancreatic adenocarcinoma is poor. The current standard of care for unresectable locally advanced pancreatic adenocarcinoma (LA-PAC) consists of chemotherapy with or without radiation[1,3] and is extrapolated from trials in metastatic or unspecified advanced disease.[4–8] Gemcitabine emerged as a standard of care in 1997[4]; the addition of nab-paclitaxel to gemcitabine improved median overall survival (OS) to 8.5 months.[7] First-line FOLFIRINOX increased OS to 11.1 months in metastatic Q4 disease but is recommended for patients with good performance status because of significant toxicities.[1,3,6] Novel therapies for advanced pancreatic adenocarcinoma have mostly been investigated in metastatic populations and less so in LA-PAC.[9–11] Targeted agents and immunotherapies such as erlotinib, olaparib, and pembrolizumab have limited Q5

Check out the accompanying podcast, “TTFields in Locally Advanced Pancreatic Adenocarcinoma,” with Drs. Eileen M. O’Reilly and Peter Li, located on the online publication’s main page or at asco.org/podcasts.

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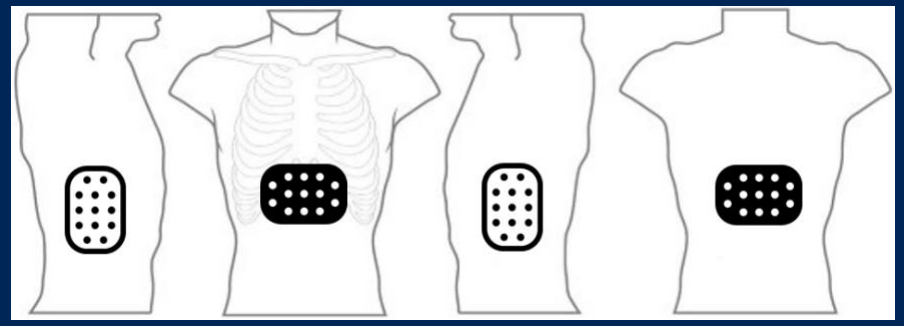
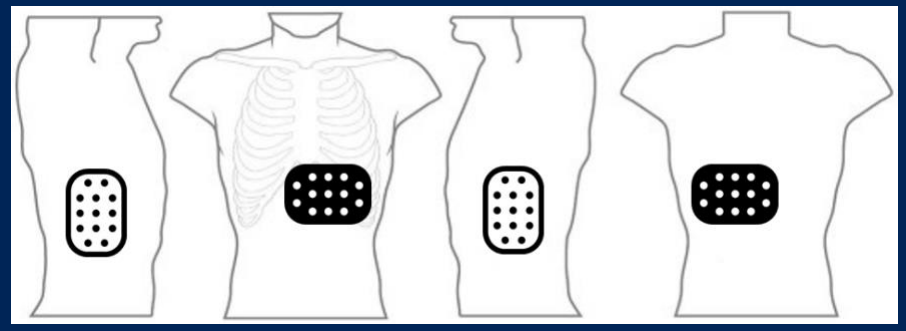
Appendix

Array Layouts

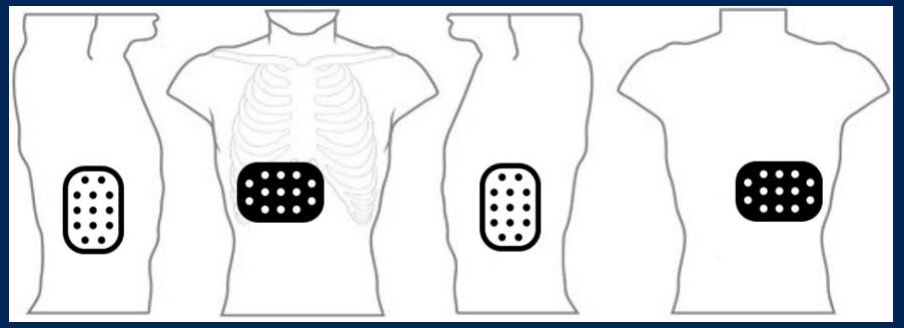
A) Epigastric-centered with the superior discs row at the level of the xiphoid



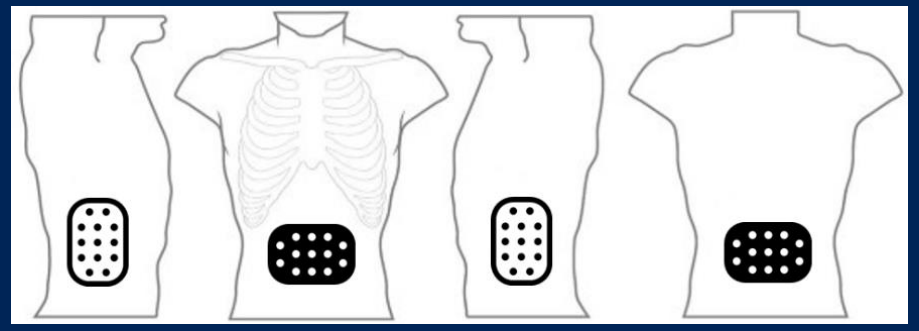
B) Left hypochondriac-shifted to the left with the superior discs row at the level of the xiphoid



C) Right hypochondriac-shifted to the right with the superior discs row at the level of the xiphoid

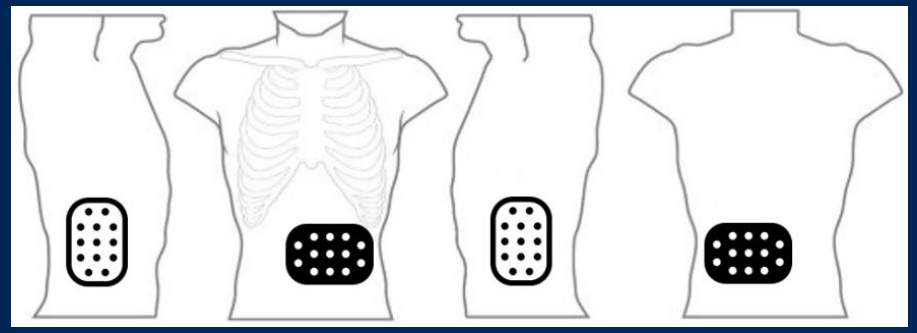


D) Umbilical- centered with the superior discs row at the inferior border of the 10th costal cartilage

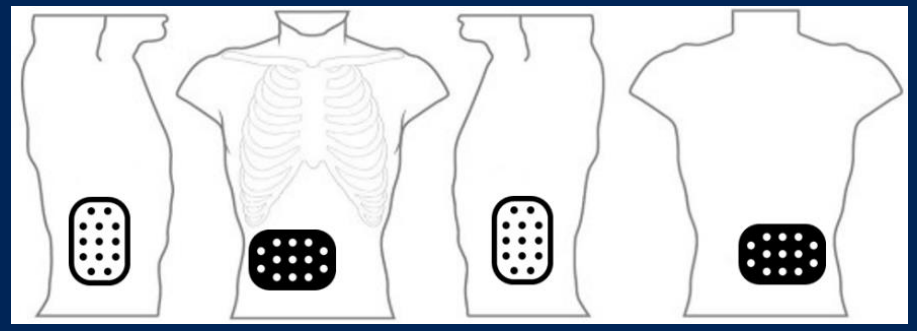


Array Layouts – continued

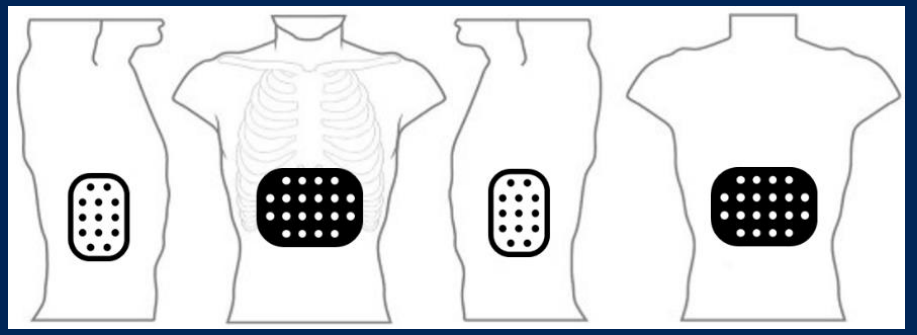
E) Left lumbar-shifted to the left with the superior discs row at the inferior the 10th costal cartilage



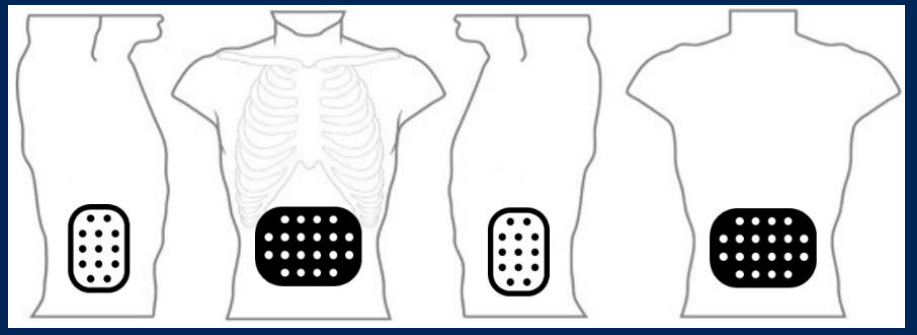
F) Right lumbar-shifted to the right with the superior discs row at the inferior border of the 10th costal cartilage.



G) Large epigastric- centered with the superior discs row at the level of the xiphoid



H) Large umbilical- centered with the inferior discs row below the umbilicus



Secondary Endpoints in the mITT population

PFS

mITT	TTFields + GnP	GnP	P-value
Median PFS (95% CI) **Events**	11.2 (9.4, 13.1) 136	10.7 (9.1, 11.5) 121	**0.183**
	HR = 0.84 (95% CI: 0.66, 1.08)		
1-year PFS rate, median (95% CI)	48.5 (40.5, 56.0)	38.7 (30.5, 46.8)	0.044

Distant PFS (post-hoc)

mITT	TTFields + GnP	GnP	P-value
Median distant PFS (95% CI) **Events**	15.6 (13.1, 18.4) 81	12.2 (11.3, 13.7) 88	**0.017**
	HR = 0.69 (95% CI: 0.51, 0.94)		
1-year distant PFS rate, median (95% CI)	64.4 (55.7, 71.8)	52.6 (43.4, 60.9)	**0.013**

Local PFS

mITT	TTFields + GnP	GnP	P-value
Median local PFS (95% CI) **Events**	12.9 (11.3, 15.1) 117	11.5 (9.8, 13.1) 101	**0.194**
	HR = 0.84 (0.64. 1.10)		
1-year local PFS rate, median (95% CI)	51.9 (44.8, 58.6)	41.8 (34.2, 49.2)	0.027

Pain-free survival

mITT	TTFields + GnP	GnP	P-value
Median pain-free survival (95% CI) **Events**	16.6 (11.0, 29.9) 79	9.2 (7.6, 12.9) 86	**0.019**
	HR = 0.69 (95% CI: 0.50, 0.94)		
1-year pain-free survival rate, Median (95% CI)	56.8 (48.1, 64.7)	45.8 (36.6, 54.6)	**0.040**

Overall response rate (ITT population)

- ORR and resectability rate were not significantly improved with concomitant TTFields therapy
- Resectability rate was comparable to other trials in this population

	TTFields + GnP (n=244)	GnP (n=243)
Best overall response, n (%)		
CR	3 (1.2)	0
PR	85 (34.8)	73 (30.0)
SD	142 (58.2)	150 (61.7)
PD	14 (5.7)	20 (8.2)
ORR, % (95% CI)	**36.1 (30.0, 42.4)**	**30.0 (24.3, 36.2)**
Mean difference in ORR, % (95% CI)	6.0 (−2.4, 14.4)	
1-sided p-value	**0.094**	
Resectability rate, % (95% CI)	7.0% (4.3, 10.6)	10.1% (6.9, 14.2)

CI, confidence interval; CR, complete response; GnP, gemcitabine/nab-paclitaxel; ITT, intent-to-treat population; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; TTFields, Tumor Treating Fields

Salvage Therapies

Summary of Salvage Systemic Therapies	TTFields + GnP (N=285)	GnP (N=286)
Number of Subjects Having Salvage Systemic Therapies	**146 (51.2)**	**134 (46.9)**
Fluorouracil	92 (32.3)	78 (27.3)
Irinotecan hydrocholide	85 (29.8)	69 (24.1)
Folinic acid	75 (26.3)	61 (21.3)
Oxaliplatin	57 (20.0)	42 (14.7)
Radiotherapy	48 (16.8)	44 (15.4)
Gemcitabine Hydrochloride	29 (10.2)	24 (8.4)
Capecitabine	27 (9.5)	23 (8.0)
Paclitaxel Albumin	22 (7.7)	11 (3.8)
Gimeracil; Oteracil; Tegafur	9 (3.2)	5 (1.7)
Investigational Antineoplastic Drugs	8 (2.8)	5 (1.7)
Traditional Medicine	3 (1.1)	4 (1.4)
Cisplatin	3 (1.1)	2 (0.7)

Limitations

- Investigator's assesment of CT scans for response determination
- While protocol included a clear definition of resectability at baseline, there was no such guidance for follow up visits
- Gender imbalance between both arms
- High discontinuation rate within the first month in both arms
- The median OS in the control arm is lower than in other phase 2 and 3 trials, albeit in line with RWE data
- Open label trial