SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Tumor Treating Fields
Device Trade Name:	Optune Pax™
Device Product Code:	SHC
Applicant's Name and Address:	Novocure GmbH 21 Neuhofstrasse 6340 Baar Switzerland
Date(s) of Panel Recommendation:	Not Applicable
Premarket Approval Application (PMA) Number:	P250034
Date of FDA Notice of Approval:	2/11/2026

Breakthrough Device: Granted Breakthrough Device status December 13, 2024 because the device and proposed indications for use met the Breakthrough Device criteria.

II. INDICATIONS FOR USE

Optune Pax™ is intended for the treatment of adult patients with locally advanced pancreatic cancer, concomitant with gemcitabine and nab-paclitaxel.

III. CONTRAINDICATIONS

- Optune Pax™ is contraindicated in patients with an electrical implant. Use of Optune Pax™ together with electrical implants has not been tested and may lead to malfunctioning of the implanted device.

- Optune Pax™ is contraindicated to patients who are sensitive to gels like the gel used on electrocardiogram (ECG) stickers or transcutaneous electrical nerve stimulation (TENS) electrodes. In this case, skin contact with the gel used with Optune Pax™ may commonly cause increased redness and itching, and rarely may even lead to severe allergies such as a fall in blood pressure and breathing difficulty.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Optune Pax™ Instructions for Use (IFU) and Patient Information and Operation Manual (PIOM).

V. DEVICE DESCRIPTION

A. Overview

Optune Pax™ is a portable, battery-powered or mains-powered device that produces alternating electrical fields, called tumor treating fields ("TTFields") within the body. TTFields are applied to the patient by non-invasive, electrically-insulated transducer arrays that are placed on the patient's abdomen and connected to the device. TTFields physically disrupt the rapid cell division exhibited by cancer cells.

Optune Pax™ delivers TTFields at 150 kHz to the entire abdomen. The device's treatment parameters are preset by Novocure. No adjustments can be made to the device by the physician or patient. Patients are initially trained on the use of the device by a Novocure device support specialist (DSS). The patient must simply learn to switch out and recharge depleted device batteries, connect to an external power supply and replace the transducer arrays at least two times per week (every 4 days at most) according to the array layout recommended by their physician.

Optune Pax™ is designed to accompany the patient throughout their daily activities for continuous treatment, with short breaks for personal needs such as to shower or replace the arrays. Patients can carry the device and battery in the specially designed bag provided as part of the treatment kit, to receive continuous TTFields treatment without changing their daily routine.

During treatment, the Optune Pax™ device records and stores technical information in an internal log file, including usage time as well as any errors or technical issues that might have occurred during treatment (e.g., inadequate contact of the transducer arrays to the abdomen of the patient).

B. Technological Characteristics

Optune Pax™ is comprised of an Electric Field Generator (the device), Insulated Transducer Arrays (transducer arrays), and several additional components, including a power supply, battery, battery charger, connection cable and carrying bag, that together comprise the Optune Pax™ Treatment Kit. An illustration of the Treatment Kit is provided in **Figure 1**, below.

1. Electric Field Generator (Optune Pax device)
2. Battery Charger
3. Power Supply and Cord
4. Connection Cable and Box (CAD)
5. Battery
6. Small Transducer Array
7. Large Transducer Array

Figure 1. Optune Pax™ Treatment Kit

Electric Field Generator: The Electric Field Generator produces TTFields per the pre-set output parameters presented below in **Table 1**. The intensity and frequency of the TTFields, as well as the maximum allowable temperature of the transducer arrays, are controlled by two microcontrollers that run on the embedded Novocure software.

Table 1. Electric Field Generator Output Parameters

	Output Parameter
Output Frequency	150 kHz
Output Current	1.414 A_{RMS}

The front panel of the Electric Field Generator is a simple user interface consisting of a socket to connect the CAD, a few simple visual indicators for Device, Battery and Error status and a TTFields ON/OFF button and Battery Test button. The back panel of the device houses the Power Supply Port and the Power switch for the device.

During treatment, the device records and stores technical information in log files, for review by Novocure personnel, including usage time of the device as well as any errors or technical issues that might have occurred during treatment. These log files can be downloaded directly by a Novocure device technician by physically connecting the Electric Field Generator to a Novocure laptop with dedicated software. Alternatively, patients can download and transmit the log files to

Novocure's secure servers via a cellular network, using MyLink, an optional data transfer unit.

Transducer Arrays: To deliver TTFields therapy, two sets of transducer arrays (4 in total) are placed on the skin of a patient's abdomen, and connected to the Electric Field Generator. Transducer array are available in two sizes to accommodate different patient sizes. Large arrays contain 20 ceramic discs, while small arrays contain 13 discs. The size of the arrays chosen for a particular patient is at the physician's discretion, based upon patient size and other considerations.

Each transducer array is comprised of serially interconnected, insulated ceramic discs that are soldered to a flexible printed circuit board (PCB). The discs are housed between a layer of adhesive tape on one side (the side that adheres to the skin), and on the other, conductive hydrogel and a foam pad layer. In addition, each array contains eight thermistors that measure skin temperature beneath the array throughout treatment. As an additional safety feature, if the thermistors detect a temperature beyond 41° C, the device will automatically shut off.

Optune Pax™ is compatible with two array models: ILE Arrays and ITE Arrays. The key features of both models are identical, including the materials, location of the discs and thermistors, performance specifications and availability in two sizes (small and large). The main difference is that the shape of the ITE Array model's medical tape and PCB are slightly different to allow for more flexibility when on the abdomen.

The location of placement of transducer arrays on the abdomen is provided to the patient as an array layout map, which is specific to each patient and based on the considerations presented in Novocure's Clinical Practice Guidelines and the treating physician's medical judgement.

Additional Components and Accessories: Together with the Electric Field Generator and Transducer Arrays, the following components make up the Optune Lua Treatment Kit: Batteries, Battery Charger, Power Supply, and Connection Cable and Box (CAD). In addition, a Carrying Bag and Transducer Array Applicator are provided to patients for use with Optune Pax™.

C. Mechanism of Action

Optune Pax™ produces TTFields within the human body through transducer arrays placed on the abdomen. TTFields physically disrupt the rapid cell division exhibited by cancer cells. TTFields technology takes advantage of the special characteristics and geometrical shape of dividing cells, which make them susceptible to the effects of the TTFields. These fields alter the tumor cell polarity at an intermediate frequency (on the order of 100-300 kHz). The frequency used for pancreatic cancer is 150 kHz. Research results demonstrate both disruption of cell division up to complete cessation of the process, as well as complete destruction of the dividing cells.

In contrast, the TTFields have not been shown to have an effect on cells that are not undergoing division. Since most normal adult cells proliferate very slowly, if at all, they are hypothesized to be minimally affected by the TTFields. Testing demonstrates no differences between treated and control animals in histology of the major internal organs (including the lungs), blood examination, cardiac rhythm, body temperature, or in animal behavior. In addition, because the fields alternate so rapidly, they have no observed effect on normal quiescent cells nor do they stimulate nerves and muscles. It is noted that, because TTFields are only applied to the abdomen, they have no effect on rapidly proliferating cells in the rest of the body.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

The standard treatment for patients with locally advanced pancreatic cancer is chemotherapy.

VII. MARKETING HISTORY

Optune Pax™ has not been marketed in the United States or any foreign country. The same device for the treatment of lung cancer – Optune Lua for Non-Small Cell Lung Cancer (NSCLC) – has been available commercially in the U.S. since 2024, via approval of PMA (P230034). Optune Lua for the treatment of malignant pleural mesothelioma (MPM) has been commercially available in the U.S. under a humanitarian device exemption (HDE) since 2019 (H180002).

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects associated with the use of Optune Pax™ include:

- Treatment related skin toxicity
- Allergic reaction to the adhesive or to the gel
- Heating of the array, leading to pain and/or local skin burns
- Infection at the site where the array makes contact with the skin
- Local warmth and tingling sensation beneath the arrays
- Medical device site reaction (e.g., skin irritation, blisters)
- Muscle twitching
- Skin breakdown / skin ulcer

Please see **Section X** (below) for the specific adverse events that occurred in the pivotal clinical study.

IX. SUMMARY OF NONCLINICAL STUDIES

A. In Vitro Studies

The objective of the studies listed below in **Table 2** was to validate the effect of TTFields at 150 kHz on cancer cells *in vitro*. These studies formed the basis for Optune Pax™ output frequency for pancreatic cancer.

Table 2. ***In Vitro Studies***

Test/Setup	Purpose	Results	Conclusion
The inhibitory effect of TTFields was tested in various cultures at a range of frequencies between 50 - 500kHz.	Investigate whether there is an optimal frequency for the antimitotic effect of TTFields and identify the main parameters that may affect treatment.	The effect of TTFields is frequency-dependent with frequency inversely related to cell size.	Optimal frequency for pancreatic cancer cells is 150 kHz.
Kinetic modeling of compartmental tumor growth kinetics.	Test the time needed to achieve tumor growth reversal using TTFields.	Tumor growth reversal is seen only if TTFields are applied continuously for several weeks.	Tumor growth reversal is not immediate.
Effects of combined TTFields with chemotherapeutic agents.	Assess effects of TTFields when combined with chemotherapy commonly used to treat pancreatic cancer.	Simultaneous application of TTFields with chemotherapeutic agents enhances probable benefit of treatment as compared to the chemotherapy alone.	TTFields have an additive effect to chemotherapy in pancreatic cell *lines in vitro*.

B. ***In Vivo*** **Studies**

Novocure has conducted multiple *in vivo* animal studies to investigate the effectiveness of TTFields against orthotropic, syngeneic primary tumors, including a study of TTFields and concomitant chemotherapy in treating hamsters bearing pancreatic tumors; a study of TTFields and concomitant chemotherapy in treating mice bearing pancreatic ductal adenocarcinomas; studies of TTFields and concomitant checkpoint inhibitors in treating mice bearing Lewis lung carcinomas and subcutaneous colon carcinomas; a study of TTFields effect on inhibiting metastatic spread of VX-2 tumors in New Zealand white rabbits and metastatic melanomas in mice; several studies of TTFields and concomitant chemotherapies in treating mice bearing Lewis lung carcinomas, mice with ovarian tumors, mice and rats bearing MPM tumors, and mice bearing VX-2 kidney tumors; and a study of TTFields in treating mice bearing Lewis lung carcinomas and squamous cell lung carcinomas. In all of these studies, TTFields were delivered to animals through specially-designed transducer arrays that could be placed on the body surfaces of these animals. Control animals were treated with sham arrays, delivering heat comparable to that generated by the TTFields transducer arrays. In all studies, TTFields effectiveness was demonstrated in the respective animal and tumor models.

Novocure has also conducted several safety studies in healthy rabbits and rats, including a safety study of 150 kHz TTFields applied to rat torsos, and safety studies of 150 kHz TTFields applied to rabbit torsos with concomitant chemotherapies. These studies found no treatment-related side effects when TTFields were applied alone or together with concomitant chemotherapies, thus supporting the safety of

TTFields. The reasons for the low toxicity of TTFields treatment can be explained in the light of the known passive electric properties of normal tissues within the body and the effects of electric fields applied via insulated transducer arrays.

C. Additional Studies

1. Simulations of Field Intensity Distributions

Simulations were performed to evaluate the safety and effectiveness of Optune Pax™ when delivering Tumor Treating Fields to the abdomen. A virtual representation of the Optune Pax™ was used to deliver TTFields to the abdomens of three (3) different human computational models – a female model, a male model, and an obese male model with a range of body mass index (BMI) values from normal to obese. The simulations showed that for all models, Optune Pax™ delivers therapeutic intensities to the abdominopelvic regions. Thermal safety threshold levels were determined by current density and specific absorption rate (SAR). Current density within the models was below the safety threshold of 100 mA/cm^2. SAR values within the internal organs were below the levels at which thermal damage occurs. In the superficial body layers, higher SAR values were observed. However, Optune Pax™ incorporates temperature control that prevents the skin from heating to levels at which thermal damage can occur.

2. Electrical Safety and Electromagnetic Compatibility Tests

Novocure commissioned an independent laboratory to evaluate the electrical safety and electromagnetic compatibility of Optune Pax™. The laboratory tested the device according to IEC 60601-1, IEC 60601-1-11, and IEC 60601-1-2, and found it to be free from safety hazards and in compliance with the requirements of that standard. A summary is provided below in **Table 3**.

Table 3. Electrical Safety and Electromagnetic Compatibility (EMC) Testing

Test	Purpose	Standard	Results
Safety-general	Equipment when transported, stored, installed, operated in normal use, and maintained according to the instructions of the manufacturer, causes no safety hazard which could reasonably be foreseen and which is not connected with its intended application in normal condition (NC) and in single fault condition (SFC).	IEC 60601-1	Pass
Safety-classification	Type of protection against electric shock. Internally powered equipment.	IEC 60601-1	Pass
Safety-degree of protection against electric shock	Type BF applied part.	IEC 60601-1	Pass
Safety-mode of operation	Continuous operation.	IEC 60601-1	Pass
Safety-use in	Home environment use.	IEC 60601-1-11	Pass

Test	Purpose	Standard	Results
the home environment			
Emissions	Radiated RF emissions, Class B.	EN/IEC 60601-1-2	Pass
Immunity	Immunity to electrostatic discharge (ESD). Radiated immunity to radio frequency electromagnetic field. Conducted immunity to electrical fast transients/bursts (EFT/ B). Conducted immunity to disturbances induced by radio frequency field. Radiated immunity to power frequency magnetic field, 50/60 1 Hz.	EN/IEC 60601-1-2	Pass

3. Software Verification and Validation Testing

Novocure provided software information for Optune Pax™, in accordance with FDA guidance. Optune Pax™ software documentation of appropriate controls and testing was provided, including: Level of Concern, Software Description, Device Hazard Analysis, Software Requirements Specifications, Architecture Design Chart, Software Design Specification, Traceability, Software Development Environment Description, Verification and Validation Documentation, Revision Level History, Unresolved Anomalies, and Run-Time Error Detection.

Optune Pax™ incorporates embedded device software comprised of two independent modules. The main device software module is embedded in the Electric Field Generator and controls the intensity of the tumor treating fields, the frequency of the waves, and the temperature of the transducer arrays via micro-controllers. The CAD software module is embedded within the CAD component, and provides communication from the transducer arrays to the Electric Field Generator. The device software has been fully verified and validated to meet its predefined specifications, by engineers who were not involved in the development of the software or software accessories.

In addition to the embedded device software are the NovoTerminal software and MyLink software. The NovoTerminal software resides on a Novocure computer and is used by Novocure employees to extract logfile data from devices. MyLink is used to download Optune Pax™ device log files and transmit them to Novocure's secure servers via a cellular network.

Cybersecurity risk management is performed in accordance with FDA guidance. The system's software has an overall low level of complexity and its use presents low likelihood of harm due to cybersecurity risk.

4. Biocompatibility

The transducer arrays are the only patient-contacting component of the device, and have been tested for biocompatibility in GLP-certified laboratories according to ISO 10993-1, ISO 10993-5, and ISO 10993-10. The company performed

biocompatibility endpoint assessments for cytotoxicity, skin irritation/intracutaneous reactivity, and sensitization for the transducer arrays. A summary is provided below in **Table 4**. The tests result clearly showed that no leachable substances were released in cytotoxic concentrations from the transducer arrays. Furthermore, the tests show that the arrays have no sensitizing properties and do not cause skin irritation. Based on this testing, the materials that may encounter the patient are safe and biocompatible considering the biocompatibility requirements, the nature of contact and duration.

5. Sterilization

The transducer arrays are sterilized per EN 556-1 standard for sterilization of medical devices and comply with EN/ISO 11137-1, EN/ISO 11137-2, EN/ISO 11137-3, EN/ISO 11737-1 and EN/ISO 11737-2 standards. Sterilization process validation for the ITE transducer arrays follows the same sterilization process that has been previously validated, and already approved for the ILE transducer arrays (under H180002). The tolerability of the transducer arrays to high dose gamma irradiation limit was determined to be 40 kilogray (kGy) for one irradiation cycle and the compatibility of materials with this dose was validated. Package integrity was validated and found in full compliance with ISO 11607-1, "Packaging for terminally sterilized medical devices -- Part 1: Requirements for materials, sterile barrier systems and packaging systems" and ISO 11607-2, "Packaging for terminally sterilized medical devices -- Part 2: Validation requirements for forming, sealing and assembly processes." A summary is provided below in **Table 4**.

Table 4. Biocompatibility, Sterilization, and Shelf Life – Transducer Arrays

Test	Standard/Method	Result	Conclusion
Biocompatibility testing, including cytotoxicity, skin irritation, intracutaneous reactivity, and sensitization	FDA Guidance Document: Use of International Standard ISO 10993-1 FDA recognized consensus standard ISO 10993-1	Pass: Test results showed that no leachable substances released in cytotoxic concentrations from arrays. Furthermore, the tests show that the arrays have no sensitizing properties and do not cause skin irritation.	The materials that may come in contact with the patient are safe and biocompatible considering the biocompatibility requirements, the nature of contact, and duration.
Gamma irradiation sterilization validation	Arrays sterilized per EN 556-1 and comply with EN/ISO-11137-1, EN/ISO 11137-2, EN/ISO 11137-3, EN/ISO 11737-1, and EN/ISO 11737-2	Pass	Arrays are sterile.
Shelf-Life validation	Test whether electrical and mechanical properties of the arrays remain within their specifications at the end of their shelf life.	Pass	Shelf life for the arrays is 9 months

6. Hardware, Functional and Usability Testing

The Hardware, Functional and Usability testing are summarized below in **Table 5**.

Table 5. Hardware, Functional and Usability Testing

Test	Methods / Acceptance Criteria	Results
Electric Field Generator Testing	• Measurements of dimensions and weight • Visual inspection of physical features (i.e., venting, fan, cavity for battery, battery quick release mechanism, user interface, battery temperature sensor) • Functional/durability testing of the TTFields button (36,500 cycles) • Functional/durability testing of power supply cable connection/disconnection (3650 cycles) • Functional/durability testing of CAD connection/disconnection (3650 cycles) • Watchdog circuit functional testing • Ability of the Electric Field Generator to receive accurate thermistor measurements • The ability of thermistors in the Electric Field Generator to produce accurate measurements (i.e., ±2°C) • Visual inspection/compatibility testing of connectors/ports on the Electric Field Generator • Overvoltage and overcurrent functionality testing • Signal waveform testing over a range of loads, with/without battery power • Low power hardware protection testing	PASS
Battery / Battery Charger Testing	• Measurements of dimensions and weight • Visual inspection/performance of the fuel gage buttons/indicator on the Battery • Visual inspection/performance of other Battery physical features • Performance/durability testing of Battery docking (750 cycles) • Charge carrying performance of the Battery (in the context of treatment time) and low battery error/visual indications functionality • Battery temperature testing • Battery electrical specifications testing • Battery safety testing (e.g., inclusion of a protection circuit) • Battery Charger mechanical/physical features testing • Battery Charger user interface visual inspection/functional testing (including indicators functional testing) • Battery Charger performance testing (e.g., Battery voltage over time during charging, charge current) • Battery detection testing (including faulty Battery detection)	PASS
Power Supply Testing	• Visual inspection/functional testing of the connections and indicators on the Power Supply • Electrical performance of the Power Supply	PASS
CAD Testing	• Measurements of dimensions and weight • Visual inspection of physical features (e.g., existence of shielding, existence of locking clip, microcontroller on CAD PCB)	PASS

Test	Methods / Acceptance Criteria	Results
Array Thermistor Testing	• Temperature measurements made by the thermistors are accurate to ±1°C within the range of 30 – 40°C (ILE Transducer Arrays) • Temperature measurements thermistors were accurate to ±1°C within the range of 36 – 42°C (ITE Transducer Arrays) • Temperature measurements are made every 10±1 seconds • Over-temperature alarm is triggered at temperature values greater than 41°C	PASS
Array Verification / Validation	• Visual inspection of array features • Inspection of array conductive layer using a multi-meter • Measurements made with calipers and a scale to verify masses and distances on array samples • Verification that array capacitance (i.e., between 20 – 60 nF) and resistance to DC (direct current) is within specification (i.e., less than 10MΩ) • That measured array impedance values at 30.6°C and 43.4°C are less than or equal to 19.94Ω • Measured leakage current values are less than < 10μA and array samples do not show any signs of burn damage at the ceramic discs after applying 400VDC • Measured current at each ceramic disc is greater than 230mA during 1 minute of therapy • Visual inspection of thermistors • Verification of the array strain relief and cable / connection cable box (CAD) compatibility (ITE arrays) • Testing to verify the adhesive strength of the adhesive tape and ability to peel the liner • Testing to verify a lack of mechanical/electrical damage due to bending	PASS

X. SUMMARY OF PRIMARY CLINICAL STUDY – EF-27/PANOVA-3

The applicant conducted a pivotal clinical study (EF-27/PANOVA-3) to establish a reasonable assurance of safety and effectiveness of Optune Pax™ in the treatment of adult patients with locally advanced pancreatic cancer, under IDE G170288 (NCT03377491). Data from this clinical study formed the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The EF-27/PANOVA-3 clinical study was a pivotal, randomized, open-label, two-arm, multi-center study evaluating the effectiveness and safety of TTFields, using Optune Pax™, concomitant with gemcitabine and nab-paclitaxel (GnP) for front-line treatment of locally advanced pancreatic cancer. Nab-paclitaxel and gemcitabine are chemotherapies approved for the treatment of pancreatic cancer, and are one of only a few accepted standard of care (SoC) treatments for patients with locally-advanced pancreatic cancer. Participants in the study were randomized in a 1:1 ratio to receive TTFields, concomitant with gemcitabine and nab-paclitaxel (TTFields+GnP arm), or gemcitabine and nab-paclitaxel alone (GnP arm). The

primary effectiveness endpoint in the study was overall survival (OS) of patients treated with TTFields concomitant with gemcitabine and nab-paclitaxel, compared to OS of patients treated with chemotherapy alone.

B. Clinical Inclusion and Exclusion Criteria:

1. Inclusion Criteria

Enrollment in the EF-27/PANOVA-3 study was limited to patients who met the following criteria:

1. 18 years of age and older
2. Life expectancy of ≥3 months
3. Histological/cytological diagnosis of de novo adenocarcinoma of the pancreas
4. Unresectable, locally advanced stage disease according to the following criteria (per Al-Hawary MM, et al., Radiology 201413; NCCN Clinical Practice Guidelines in Oncology)
    a. Head/uncinate process:
        i. Solid tumor contact with Super Mesenteric Artery (SMA)>180°
        ii. Solid tumor contact with the Celiac Axis (CA) >180°
        iii. Solid tumor contact with the first jejunal SMA branch
        iv. Unreconstructible SMV/PV due to tumor involvement or occlusion (can be d/t tumor or bland thrombus)
        v. Contact with most proximal draining jejunal branch into SMV
    b. Body and tail
        i. Solid tumor contact of >180° with the SMA or CA
        ii. Solid tumor contact with the CA and aortic involvement
        iii. Unreconstructible Superior Mesenteric Vein/SMV-portal vein (SMV/PV) due to tumor involvement or occlusion (can be d/t tumor or bland thrombus)
    c. No distant metastasis, including non-regional lymph node metastasis
    d. No borderline resectable (per Al-Hawary MM, et al., Radiology 201413)
5. Eastern Cooperative Oncology Group (ECOG) score 0-2
6. Amenable and assigned by the investigator to receive therapy with gemcitabine and nab-paclitaxel
7. Able to operate the NovoTTF-200T independently or with the help of a caregiver
8. Signed informed consent form for the study protocol

2. Exclusion Criteria

Patients were not permitted to enroll in the EF-27/PANOVA-3 study if they met any of the following exclusion criteria:

1. Prior palliative treatment (e.g. surgery, radiation) to the tumor
2. Cancer requiring anti-tumor treatment within the 5 years before inclusion, excluding treated stage I prostate cancer, in situ cervical or uterus cancer, in situ breast cancer and nonmelanomatous skin cancer.
3. Serious co-morbidities:
    a. Clinically significant (as determined by the investigator) hematological, hepatic and renal dysfunction, defined as: Neutrophil count <1.5 x 109/L and platelet count <100 x 109/L; bilirubin >1.5 x Upper Limit of Normal (ULN); Aspartate Aminotransferase (AST) and/or Alanine Aminotransferase (ALT) >2.5 x ULN; and serum creatinine >1.5 x ULN.
    b. History of significant cardiovascular disease unless the disease is well controlled. Significant cardiac disease includes second/third degree heart block; significant ischemic heart disease; poorly controlled hypertension; congestive heart failure of the New York Heart Association (NYHA) Class II or worse (slight limitation of physical activity; comfortable at rest, but ordinary activity results in fatigue, palpitation or dyspnea).
    c. History of arrhythmia that is symptomatic or requires treatment. Subjects with atrial fibrillation or flutter controlled by medication are not excluded from participation in the study.
    d. History of cerebrovascular accident (CVA) within 6 months prior to randomization or that is not stable.
    e. Active infection or serious underlying medical condition that would impair the ability of the subject to receive protocol therapy.
    f. History of any psychiatric condition that might impair subject's ability to understand or comply with the requirements of the study or to provide consent.
4. Concurrent anti-tumor therapy beyond gemcitabine and nab-paclitaxel
5. Implantable electronic medical devices in the torso, such as pacemakers
6. Known severe hypersensitivities to medical adhesives or hydrogel, or to one of the chemotherapies used in this study.
7. Pregnancy or breast-feeding (female subjects with reproductive potential and their partners must accept to use effective contraception throughout the entire study period and for 3 months after the end of treatment). All subjects who are capable of becoming pregnant must take a pregnancy test which is negative

within 72 hours before beginning study drug administration. The definition of effective contraception is left up to the decision of the investigator.

8. Unable to follow the protocol for medical, psychological, familial, geographic or other reasons.
9. Admitted to an institution by administrative or court order.

C. Study Arms:

The EF-27/PANOVA-3 study included two arms, as follows:

- **TTFields+GnP Arm**: Participants received Optune Pax™ together with gemcitabine and nab-paclitaxel (GnP).
- **GnP Alone Arm**: Participants received GnP without Optune Pax™.

D. Study Treatments

1. Gemcitabine + Nab-Paclitaxel (GnP)

Gemcitabine and nab-paclitaxel were administered according to their approved package inserts. Nab-paclitaxel was administered as follows: 125 mg/m2 administered as an intravenous infusion over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle, until radiological progression per Response Evaluation Criteria in Solid Tumors (RECIST) V1.1, or unacceptable toxicity based on investigator assessment. Gemcitabine was administered as follows: 1000 mg/m^2 over 30-minute infusion administered immediately after nab-paclitaxel on Days 1, 8 and 15 of each 28-day cycle until radiological progression per RECIST V1.1, or unacceptable toxicity based on investigator assessment.

2. TTFields Therapy

For study participants randomized to the TTFields+GnP Arm, TTFields therapy was delivered using Optune Pax™ (150 kHz). At treatment initiation, participants were instructed by the investigator, a designated healthcare provider or a Novocure Device Support Specialist (DSS) on how to place the transducer arrays on the abdomen, per the array layout determined by the investigator, and how to operate the device. Following this training, participants continued TTFields treatment at home.

TTFields therapy was initiated within 7 days of randomization, and ±3 days of administering GnP. Participants received uninterrupted multiple single month courses of TTFields therapy. Treatment was to be stopped in cases of intolerable toxicity or disease progression in the abdomen ("local disease progression").

The recommended transducer array layout was determined by the investigator for each participant using the *Clinical Practice Guidelines-Layout Optimization in Pancreatic Malignancies*, which was developed to maximize TTFields intensity in

the area of maximal disease burden in the abdomen (based on the patient's baseline CT scan). After being trained on how to use the device and place the arrays, participants continued TTFields therapy at home. Participants were instructed that TTFields application will be continuous for at least 18 hours a day on average and to replace the arrays two to three times per week. At array replacement, the skin was re-shaved if needed, and treated using topical steroids or antibiotic creams, if recommended. The concomitant chemotherapy, GnP, was administered as described above.

E. Follow-Up Schedule

During the treatment period, participants were seen every four weeks until local disease progression, with the following assessments performed: concomitant medication recording, ECOG performance status, physical examination (including vital signs), complete blood count including differential, serum chemistry including CA-19-9, AE and device deficiency collection and recording, documentation of ascitic fluid drainage (if applicable), pain assessment using VAS and device usage time assessment (only for subjects in the TTFields+GnP Arm. In addition, every eight weeks, the following assessments were performed until local disease progression: CT/MRI scan of the chest and abdomen, assessment of local and distant disease status per RECIST v1.1. Furthermore, European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ C30) questionnaires with the pancreatic cancer module (PAN26) addendum were completed by the participating subjects. In addition, bone scan and/or CT/MRI of the brain were performed if clinically indicated. One month following treatment discontinuation, the following assessment were performed: concomitant medications recording, ECOG performance status, physical examination (including vital signs), complete blood count including differential, serum chemistry panel including CA-19-9, AE and device deficiency collection and recording and documentation of ascitic fluid drainage were performed during this visit. In addition, following local disease progression, telephone follow-up was conducted every four weeks for survival status until study completion or death.

Table 6 below provides the full schedule of evaluations in the study.

Table 6. Study Evaluation Visit Schedule

	Screening/Baseline		**Randomization**	**Follow-up**		**Post-treatment termination visit**	**Survival follow-up**
	T=(-28)-0 days (baseline evaluation)	**T=(-14)-0 days (baseline evaluation)**	**T=0 days (randomization)**	**T=every 4 weeks prior to local progression (day 28, 56, 84, … +/- 7 days)**	**T= every 8 weeks prior to local progression (Day 56, 112, 168, … +/- 7 days)**	**T=30-37 days after discontinuing the last study treatment**	**T=every 4 weeks after local progression (Day 28, 56, 84, … post last visit +/- 7 days)**
CT Chest & Abdomen	X				X		
CT/MRI of brain (if clinically indicated)	X				X		
Bone scan (if clinically indicated)	X				X		

	Screening/Baseline		Randomization	Follow-up		Post-treatment termination visit	Survival follow-up
	T=(-28)-0 days (baseline evaluation)	**T=(-14)-0 days (baseline evaluation)**	**T=0 days (randomization)**	**T=every 4 weeks prior to local progression (day 28, 56, 84, … +/- 7 days)**	**T= every 8 weeks prior to local progression (Day 56, 112, 168, … +/- 7 days)**	**T=30-37 days after discontinuing the last study treatment**	**T=every 4 weeks after local progression (Day 28, 56, 84, … post last visit +/- 7 days)**
Medical history		X					
Performance status (ECOG score)		X		X	X	X	
Physical examination		X		X	X	X	
Pain assessment (VAS)		X		X	X		
Documentation of ascitic fluid drainage		X		X	X	X	
Complete blood count, including differential		X		X	X	X	
Serum chemistry panel		X		X	X	X	
CA 19-9 blood test		X		X	X	X	
Coagulation tests (Prothrombin time/International Normalized Ratio (PT/INR), Partial thromboplastic time (PTT))		X					
Serum Pregnancy Test (within 72 hours prior to first study drug administration)		X (if applicable)					
Randomization			X				
Adverse Events and device deficiency				X	X	X	
Concomitant medication		X		X	X	X	
EORTC QLQ C30 questionnaire + PAN26 addendum questionnaire		X			X		
Tumor assessment	X				X		
NovoTTF-200T Usage time assessment				X (if applicable)	X (if applicable)		
TTFields Therapy				X (if applicable)	X (if applicable)		
Gemcitabine & Nab-Paclitaxel				X (if applicable)	X (if applicable)		
Telephone /Visit Follow up for survival							X
Signed Informed Consent Form (ICF)	X						

F. Study Schema:

The study schema for the EF-27/PANOVA-3 study is illustrated in **Figure 2**, below.

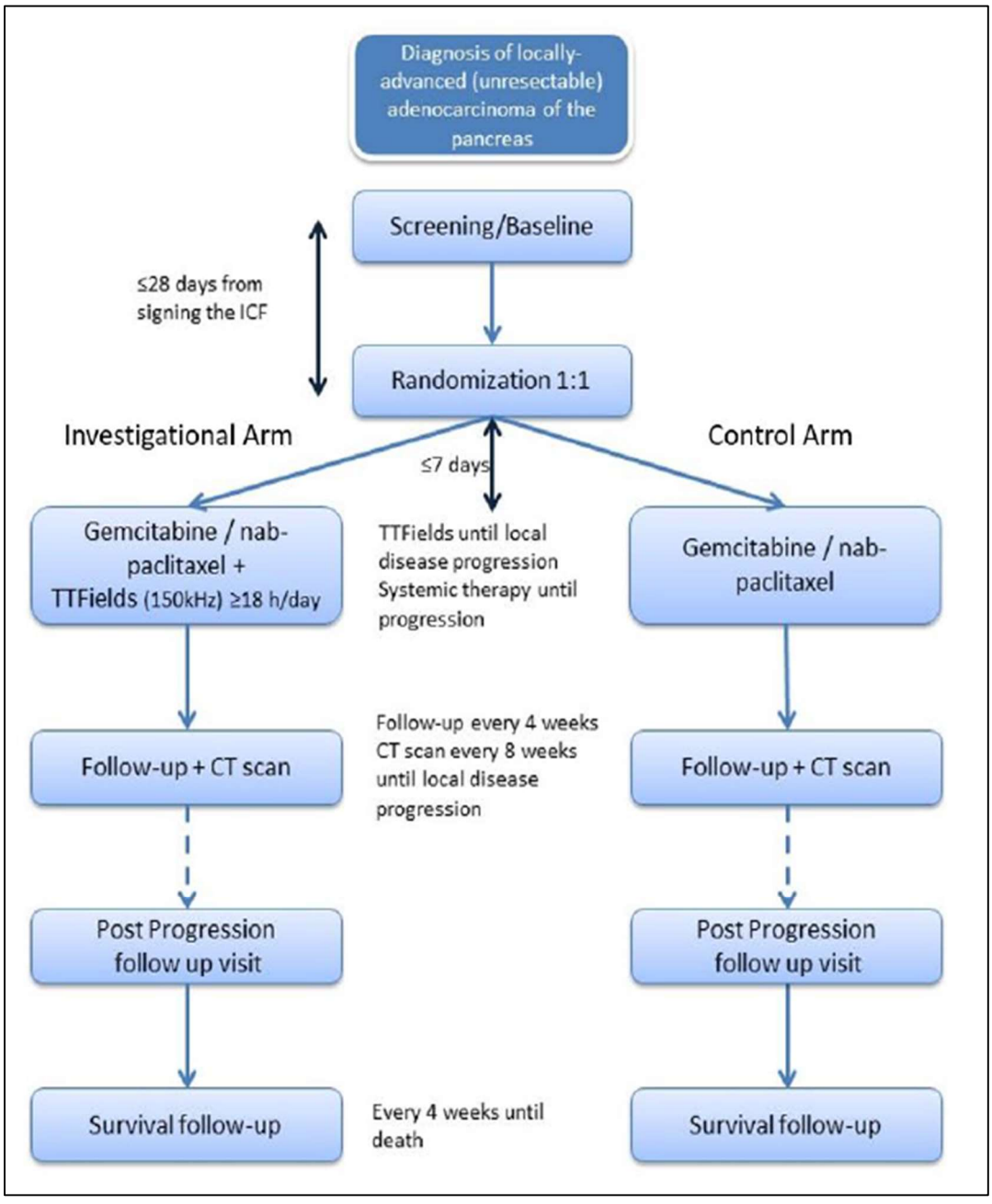


Figure 2. EF-27/PANOVA-3 Study Schema

G. Clinical Endpoints:

The primary effectiveness endpoint of the study was the following:

- Overall Survival (OS) of participants treated with TTFields concomitant with gemcitabine and nab-paclitaxel, compared to OS of patients treated with gemcitabine and nab-paclitaxel alone (superiority).

  OS was measured from the date of randomization to the date of death (in months). At the time of analysis, patients lost to follow-up or still on protocol follow-up were censored at the last date when they were known to be alive (administrative censoring).

The key secondary effectiveness endpoint of the study was the following:

- Progression-free survival (PFS) of participants treated with TTFields concomitant with gemcitabine and nab-paclitaxel, compared to PFS of patients treated with gemcitabine and nabpaclitaxel alone (superiority).

  PFS was defined as the time from the date of randomization until the date of disease progression for the entire body or death. Progression of the disease was assessed per revised RECIST Criteria Version 1.1.

  In the ITT analysis, all observed disease progression assessments were included as events in the PFS analysis, regardless of intermittent missing assessments. Deaths which occurred after the last tumor assessment without progression were considered events if they occur within 16 weeks (two missed disease assessments) after the last tumor assessment. Deaths which occurred after two or more (≥2) consecutive missed disease assessments were censored at the last tumor assessment date or randomization date, the latter of the two. Patients who had not progressed or died at time of analysis or were with unknown progression and death status were censored at the last date of their evaluable RECIST assessment or randomization date, the latter of the two. Patients who have no post baseline tumor assessment was censored at their randomization date.

The following additional secondary endpoints were measured in the study:

- Local PFS of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel.

  Local PFS was defined as the time from the date of randomization until the date of local disease progression or death. Local disease progression is defined as progressive disease per revised RECIST V1.1 in the absence of distant metastasis, including non-regional lymph node metastasis, i.e., at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on the study). The appearance of one of more new local lesions is also considered progression.

In the ITT analysis, all observed local disease progression assessments were included as events in the local PFS analysis, regardless of intermittent missing assessments. Deaths which occurred after the last tumor assessment without local progression were considered events if they occur within 16 weeks (two missed disease assessments) after the last tumor assessment. Deaths which occurred after two or more (≥2) consecutive missed disease assessments were censored at the last tumor assessment date or randomization date, the latter of the two. Patients who had not progressed or died at the time of analysis or were with unknown progression and death status were censored at the last date of their evaluable RECIST assessment or randomization date, the latter of the two. Patients who have no post baseline tumor assessment were censored at their randomization date.

- Objective response rate (ORR) of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel.

  ORR was measured as the proportion of patients with partial or complete response between the time of randomization and the time of death according to the revised RECIST Criteria V1.1. Analysis of the ORR was performed based on disease evaluation by the investigator according to RECIST v1.1.

- 1-year survival rate of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nabpaclitaxel.

- Quality of life (QoL) of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nabpaclitaxel.

  Health-Related Quality of Life (HRQoL) was measured at baseline and every 8 weeks using the EORTC QLQ C-30 questionnaire and PAN26 module (Pancreatic Cancer). HRQoL was compared between groups for each scale in the questionnaire. Subjects who experienced local disease progression were not evaluated for HRQoL endpoints following progression. Consequently, these results do not capture the quality of life status of patients with local disease progression.

- Time to Pain Progression of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nabpaclitaxel.

  Time to pain progression was defined as the duration between the time of randomization until a ≥20-point increase from baseline in a patient self-reported visual analogue scale (VAS) was recorded or death, whichever occurred first. Subjects who experienced local disease progression were not evaluated for this endpoint post-progression. In the Kaplan-Meier analysis, local disease progression, pain progression, and death were treated as events.

- Puncture-free survival of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nabpaclitaxel.

Puncture-free survival was defined as the duration between randomization until the first need for paracentesis or death, whichever occured first. Patients who experienced local disease progression were not followed for subsequent puncture events. In the Kaplan-Meier analysis, local disease progression, puncture events, and death were treated as events.

- Resectability rate of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nabpaclitaxel.

  Resectability rate was measured as the percentage of patients whose tumors were deemed resectable, defined as subjects who underwent any of the following salvage procedures: Pancreaticoduodenectomy, Pancreatectomy, Pancreatic operation, Pancreaticosplenectomy, or Tumor Excision. Resectability rate was measured as a percentage of patients whose tumors were deemed resectable by a multi-disciplinary team (MDT) consisting of at least a surgeon, a medical oncologist, and a radiologist, prior to local disease progression as defined in the protocol.

- Toxicity profile of TTFields+gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel.

The safety endpoint of the study was the following:

- Adverse events, severity and frequency in participants treated with TTFields and gemcitabine plus nab-paclitaxel compared to participants treated with gemcitabine plus nab-paclitaxel alone. Adverse events were collected and recorded based on the revised Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

H. Pivotal Study Statistical Analysis Plan and Analysis Populations

1. Analysis Datasets

The following pre-specified analysis populations were used to evaluate the study results:

- Intent to Treat (ITT): Includes all randomized participants, regardless of whether the treatment was received. Participants were analyzed according to their randomized treatment.

- Safety Population: Includes all participants who received any amount of TTFields or gemcitabine or nab-paclitaxel in the Investigational Arm, and any amount of gemcitabine or nab-paclitaxel in the Control Arm. Participants were analyzed according to actual treatment they received.

2. Statistical Hypotheses

A hierarchical approach was used to first test the primary endpoint of overall survival (OS), followed by the secondary endpoint of progression-free survival (PFS) to avoid issues related to statistical multiplicity. No other secondary endpoints were included in the testing hierarchy.

The primary endpoint was to compare overall survival (OS) of patients treated with TTFields concomitant with standard of care of chemotherapy (SOC) versus patients treated with SOC alone. The null hypothesis was that the OS is the same in the two study groups (i.e., $S_{test}(t) = S_{control}(t)$). The alternative hypothesis is that the OS is not the same (i.e., $S_{test}(t) \neq S_{control}(t)$, where $S_{test}(t)$ and $S_{control}(t)$ are the overall survival distribution of the test and control arm).

The primary endpoint was to be summarized using Kaplan-Meier (KM) estimate. The treatment difference was to be tested using a stratified two-sided log rank test with an alpha of 0.04794 in the ITT population in order to allow for two efficacy analyses of the primary endpoint (interim analysis and final analysis). The alpha level used at each time point was calculated according to the Lan-DeMets method using the O'Brien and Fleming spending function (approximately 0.0065 at the interim analysis and 0.04794 at the final analysis).

The effect of TTFields concomitant with SOC over SOC was estimated using a stratified Cox Proportional Hazard model. A hazard ratio with 95% Confidence Interval (CI) and p-value was estimated. The stratified variables were based on two stratification factors according to data from the Interactive Voice Response System (IVRS): ECOG performance status and region.

Per the statistical analysis plan (SAP), the primary endpoint was to be tested on the ITT population.

The secondary endpoint of PFS was tested only if the primary endpoint of OS met its significance level. Thus, the entire alpha of 0.05 would be allocated to the PFS endpoint, and no adjustment would be made for multiple hypothesis testing.

For PFS, a two-sided stratified log rank test at an alpha level of 0.05 was used to compare the difference of PFS between the patients treated with TTFields concomitant with SOC and the patients treated with SOC alone. The stratification factors are ECOG performance status and region. If any strata have less than 10 events, ECOG stratification factor was removed from the analysis.

The effect of TTFields concomitant with SOC over SOC alone on PFS was also estimated using a stratified Cox Proportional Hazard model. If any stratum has less than 10 events, ECOG stratification factor was removed from the analysis. The 95% confidence interval and p-value of hazard ratio were presented.

Per the SAP, this endpoint was to be tested on the ITT population.

I. Accountability of PMA Cohort

The first study participant was enrolled on May 15, 2018. The last participant was enrolled on March 9, 2023, with the last subject visit (LSLV) occurring on October 16, 2024. Ultimately, 138 sites (53 sites in North America [51 US; 2 Canada]; 18 sites in Eastern Europe/Israel; and 67 rest of world (ROW)) randomized 571 participants globally.

1. Patient Disposition

Seven hundred fifty-three (753) patients were screened and evaluated for eligibility for the study. One hundred eighty-two (182) participants were screen failures. Two hundred seventy-four (274/285, 96%) participants were randomized to the Investigational Arm and received at least one of the interventions. Additionally, three (3/285, 1%) were randomized to the Investigational Arm but received only gemcitabine and nab-paclitaxel. Two hundred seventy (270/286, 94%) participants were randomized to the Control Arm and received the allocated gemcitabine and nab-paclitaxel intervention. Following randomization to the Control Arm, 16 participants did not receive study treatment, versus only 8 participants from the Investigational Arm. Patient disposition is summarized in **Figure 3** below.

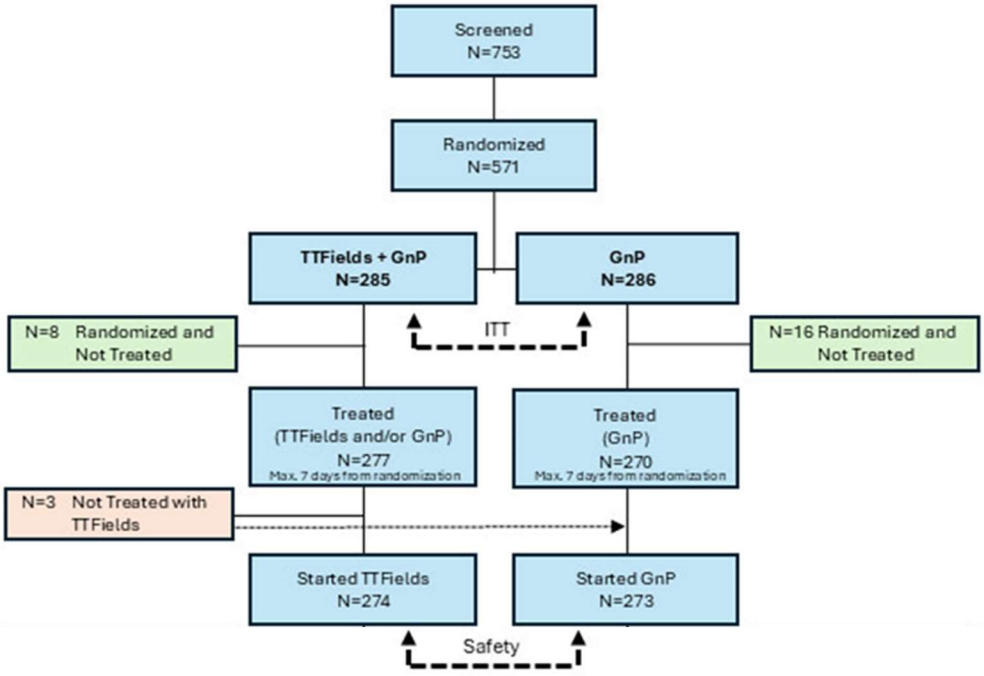


Figure 3. Patient Disposition

2. Subject Accountability

The study included 571 participants with a minimum 18 months of follow-up. Vital status accountability for the study population is presented in **Table 7** below.

Table 7. Patient Disposition for Primary Analysis (ITT)

Treatment Arm	TTFields+GnP N= 285	GnP Alone N=286	Overall N=571
Vital Status Accountability For Primary Analysis, n (%)			
Death	201 (70.5%)	230 (80.4%)	431 (75.5%)
Lost to Follow-Up	1 (0.4%)	3 (1.0%)	4 (0.7%)
Withdrawal of Consent	37 (13.0%)	14 (4.9%)	51 (8.9%)
Study Closure	39 (13.7%)	37 (12.9%)	76 (13.3%)
Other	7 (2.5%)	2 (0.7%)	9 (1.6%)

J. Study Population Demographics and Baseline Parameters

As can be seen in **Table 8** and **Table 9** below, baseline characteristics were well balanced between treatment groups. Overall, participants' median age was 67 years (range: 31-90 years), with 3.9% ECOG performance score of 2, 57.6% with score of 1 and 38.5% with score of 0. The median time from diagnosis to study enrollment was 3.6 weeks (range: 0.1- 53.7).

Compliance to the study treatments was evaluated by TTFields therapy usage for the TTFields+GnP treatment group (**Table 10**), in addition to GnP usage for both study groups (**Table 11**). The median duration of TTFields therapy was 27.6 weeks (range 0.1-234.4 weeks). The average daily usage of TTFields therapy was 59.3% (10.7 hours), median usage was 62.1% (11.2 hours), and the range was 0.1% - 99% (0.0-17.8 hours). The most frequent reason for device discontinuation was local disease progression (per protocol).

In the GnP Alone arm, duration of exposure to gemcitabine was 22.1 weeks (range: 0.1-134.1 weeks) and 21.4 weeks to nab-paclitaxel (range: 0.1-134.1 weeks). In the TTFields+GnP arm, the median duration of exposure to gemcitabine was 24.1 weeks (range: 0.1-232.4 weeks) and 23.0 weeks to nab-paclitaxel (range: 0.1-232.4 weeks). This corresponds to a median of 6.0 gemcitabine cycles (range: 1.0- 57.0 cycles) and median of 6.0 nab-paclitaxel cycles (range: 1.0-57.0 cycles) in the investigational treatment group and 6.0 gemcitabine cycles (range: 1.0-30.0 cycles) and median of 5.0 nab-paclitaxel cycles (range: 1.0-30.0 cycles) in the GnP alone group.

In terms of the overall exposure of GnP for the entire study duration, 99.8% of the safety participants discontinued gemcitabine and 99.5% discontinued nab-paclitaxel during the study. The most common reason for discontinuation of both systemic treatments was disease progression or clinical deterioration (approximately 35% in the overall cohort).

Table 8. Demographics and Baseline Characteristics – ITT Population

	TTFields+GnP (N=285)	GnP Alone (N=286)	Overall (N=571)
Age (Years)			
Median (range)	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)
Native Hawaiian or Other Pacific Islander	0	0	0
White	202 (70.9)	204 (71.3)	406 (71.1)
Other	3 (11)	5 (1.7)	8 (1.4)
Not Reported	11 (3.9)	15 (5.2)	26 (4.6)
Ethnicity, n (%)			
Hispanic or Latino	32 (11.2)	22 (7.7)	54 (9.5)
Not Hispanic or Latino	238 (83.5)	247 (86.4)	485 (84.9)
Not Reported/Unknown	15 (5.3)	17 (5.9)	32 (5.6)
Region, n (%)			
North America	123 (43.2)	125 (43.7)	248 (43.4)
Eastern Europe	43 (15.1)	42 (14.7)	85 (14.9)
Western Europe and Israel	62 (21.8)	61 (21.3)	123 (21.5)
Rest of the World	57 (20.0)	58 (20.3)	115 (20.1)
ECOG Performance Status, 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)
BMI Group, n (%)			
< 25 kg/m^2	166 (58.2)	174 (60.8)	340 (59.5)
≥ 25 kg/m^2	117 (41.1)	108 (37.8)	225 (39.4)
CA-19.9, n (%)			
Low (≤37 U/mL)	48 (16.8)	44 (15.4)	92 (16.1)
Moderate (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)
Target Lesion Site, n (%)			
Head of Pancreas	164 (57.5)	160 (55.9)	324 (56.7)
Body of Pancreas	82 (28.8)	81 (28.3)	163 (28.5)
Tail of Pancreas	9 (3.2)	19 (6.6)	28 (4.9)
Other	55 (19.3)	49 (17.1)	104 (18.2)
Multiple regions in pancreas	26 (9.1)	22 (7.7)	48 (8.4)
Extra-pancreatic	29 (10.2)	27 (9.4)	56 (9.8)

Table 9. Pancreatic Cancer History – ITT Population

	TTFields+GnP (N=285)	GnP Alone (N=286)	Overall (N=571)
Time Since Initial Pathological Diagnosis (weeks) Median (range)	3.7 (0.1, 53.7)	3.6 (0.1, 21.4)	3.6 (0.1, 53.7)

Table 10. TTFields Therapy Duration

	TTFields + GnP (N=274)
Duration of Exposure (weeks)	
Median (range)	27.6 (0.1, 234.4)
Average Usage (%)	
Mean (SD)	59.3 (21.2)
Median (range)	62.1 (0, 99)
Average Usage, n (%)	
≤75% (i.e., ≤ 13.5 hours)	200 (73.0)
>75% (i.e., ≥ 13.5 hours)	74 (27.0)
Reason for TTFields Discontinuation, n (%)	
Investigator Decision	33 (13.1)
Subject Request (Excluding Intolerable Toxicity)	60 (23.8)
Lack of Compliance	4 (1.5)
Intolerable Toxicity	4 (1.5)
Local Disease Progression (Per Protocol)	83 (30.5)
Death	11 (4.0)
Withdrawal of Consent	22 (8.0)
Adverse Event	22 (8.0)
Pregnancy	0
Other*	32 (12.7)
Unknown	3 (1.1)

*Other includes reasons such as distal progression and study closure.

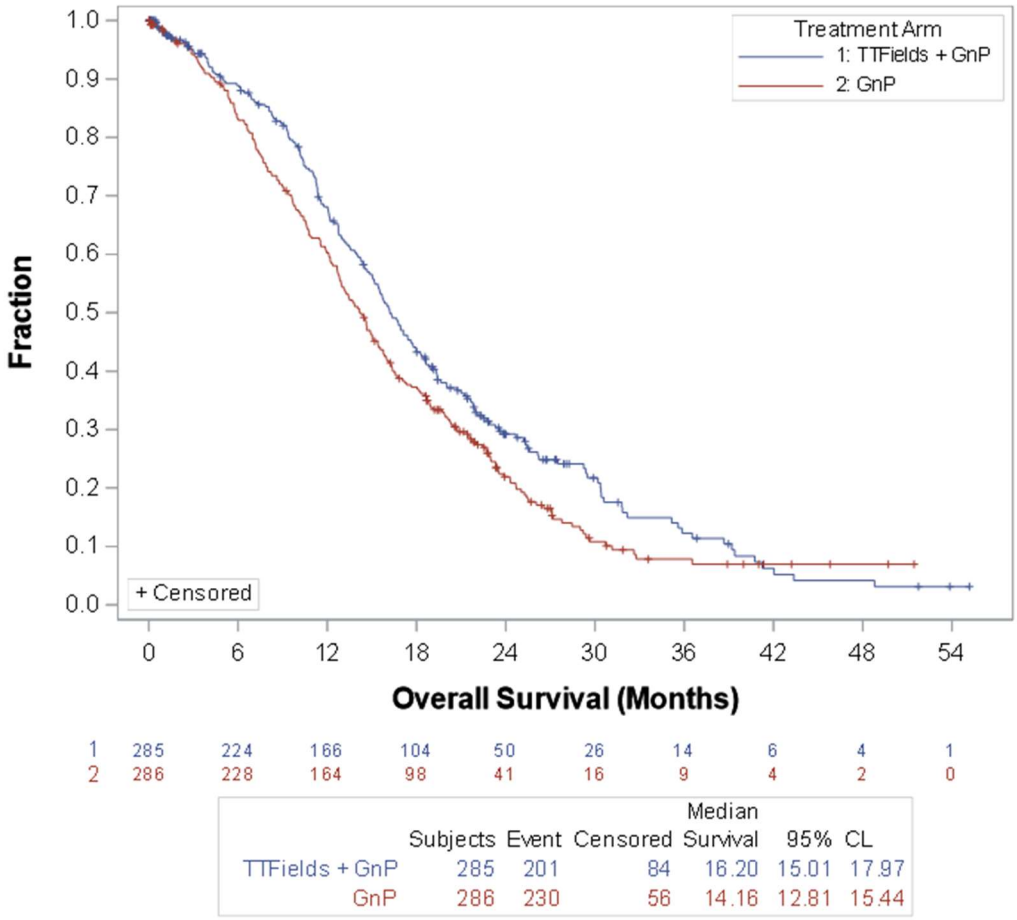
Table 11. Exposure to GnP by Study Arm (Safety Population)

	TTFields + GnP (N=274)	GnP Alone (N=273)
Gemcitabine Number of Cycles Received Median (range) **Duration of Exposure (weeks)** Median (range)	6.0 (1.0, 57.0) 24.1 (0.1, 232.4)	6.0 (1.0, 30.0) 22.1 (0.1, 134.1)
Nab-paclitaxel Number of Cycles Received Median (range) **Duration of Exposure (weeks)** Median (range)	6.0 (1.0, 57.0) 23.0 (0.1, 232.4)	5.0 (1.0, 30.0) 21.4(0.1, 134.1)

K. Effectiveness Results

1. Primary Effectiveness Endpoint – Overall Survival

Overall Survival (ITT): The primary endpoint of the study was met. The difference in OS between study arms at the final analysis in the ITT population had a probability value of p = 0.039, which met the threshold for statistical significance pre-defined as p=0.04794 per log rank test. The median OS in the TTFields+GnP arm was 16.2 months (95% CI 15.0-18.0) compared to 14.2 months (95% CI 12.8-15.4) in the GnP Alone arm (Refer to Figure 4 and Table 11). The hazard ratio (HR) for OS was 0.82 (95% CI 0.68 – 0.99). See **Figure 4** and **Table 12.**



	Subjects	Event	Censored	Median Survival	95% CL	
TTFields + GnP	285	201	84	16.20	15.01	17.97
GnP	286	230	56	14.16	12.81	15.44

Figure 4. Overall Survival (ITT)

Table 12. Median Overall Survival (TTFields+GnP vs. GnP Alone)

	TTF + GnP N= 285	GnP N=286
N of pts with event (%)	201(70.5%)	230 (80.4%)
Median in months (95% CI)	16.2 (15.0, 18.0)	14.2 (12.8, 15.4)
Hazard ratio[a] (95% CI)	0.82 (0.68, 0.99)	
P value[b]	0.039	

[a]The Hazard Ratio and its 95% CI were estimated using a stratified Cox Proportional Hazard model
[b] P-Value (2-sided) was calculated using a stratified log-rank test.

2. Key Secondary Effectiveness Endpoint – Progression-Free Survival

Progression Free Survival (ITT):

Treatment with TTFields+GnP showed no statistically significant improvement in PFS compared to GnP Alone (log rank test p = 0.137). The hazard ratio was 0.85 (95% CI 0.68 – 1.05). Median PFS was 10.6 months (95% CI: 9.2 – 12.2) with TTFields+GnP compared to 9.3 months (95% CI: 7.6 – 11.1) with GnP Alone (**Figure 5**).

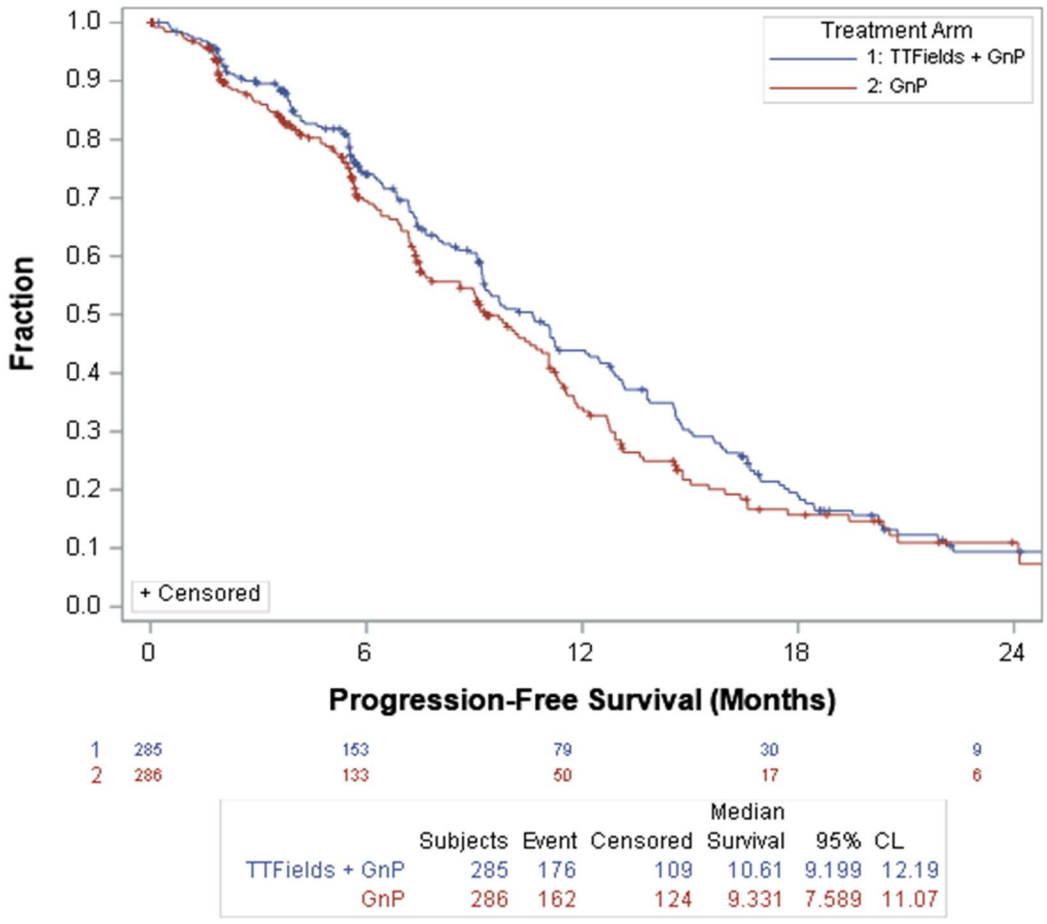


Figure 5. Progression-Free Survival (ITT)

3. Additional Secondary Endpoints

Note: Aside from Local Progression Free Survival (ITT), the remainder of the secondary endpoints were observational (i.e., there were no pre-specified statistical hypotheses or tests associated with these secondary endpoints).

Local Progression Free Survival (ITT):

Median local PFS according to RECIST v1.1 was 12.5 months [95% CI: 10.7 – 14.5] in the TTFields+GnP alone arm and 10.4 months [95% CI: 9.1 – 11.8] in the GnP alone arm (**Figure 6).**

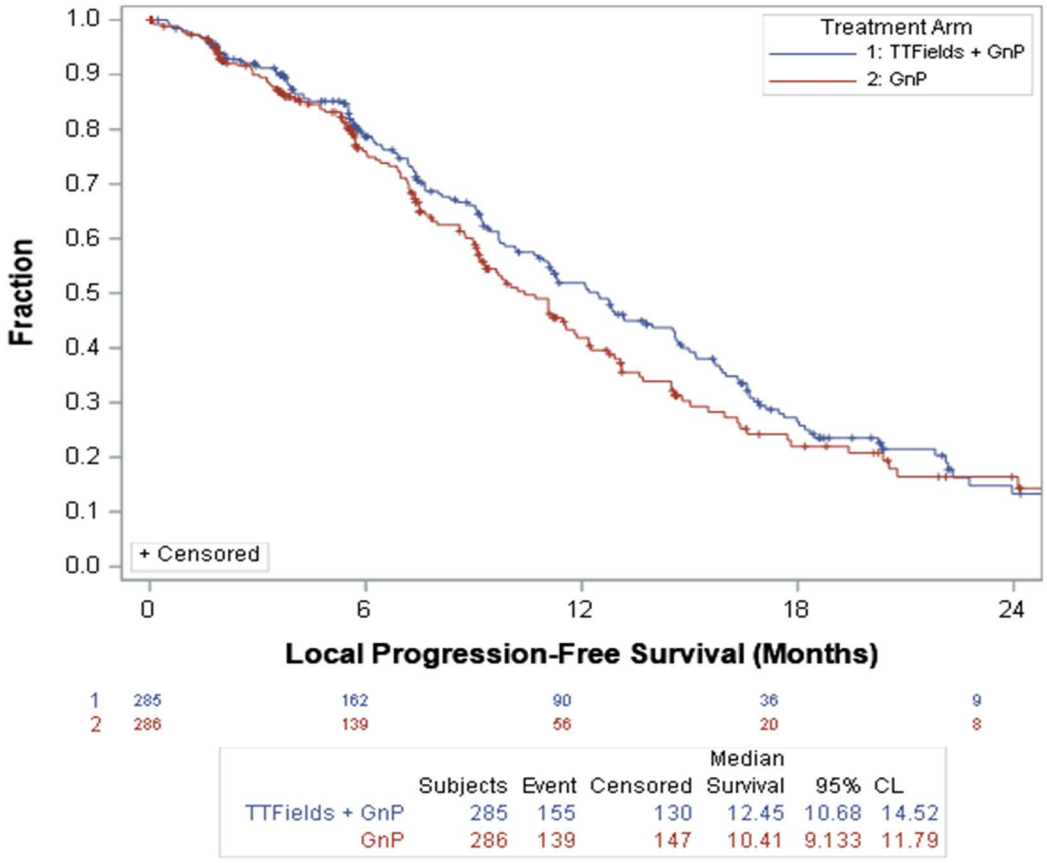


Figure 6. Local Progression-Free Survival (ITT)

Objective Response Rate (ITT with a CT scan after baseline):

In the ITT population, 244 participants in the TTFields+GnP Arm and 243 participants in the GnP Alone Arm had at least one evaluable CT scan after baseline. Of these patients, complete and partial responses in the TTFields+GnP Arm were observed in 3 (1.2%) and 85 (34.8%) participants, respectively, compared to 0 (0%) and 73 (31%) participants, respectively in the GnP Alone Arm. The ORR was 36.1% in the TTFields+GnP Arm compared to 30.0% in the GnP Alone Arm. The results are summarized in **Table 13**.

Table 13. Objective Response Rate (ITT with a CT Scan After Baseline)

Parameter	TTFields + Gemcitabine + Nab-paclitaxel (N=285)	Gemcitabine + Nabpaclitaxel alone (N=286)
Subjects with Best Overall Response*, n (%)	244	243
Complete Response (CR)	3 (1.2)	0
Partial Response (PR)	85 (34.8)	73 (30.0)
Stable Disease (SD)	142 (58.2)	150 (61.7)
Progressive Disease (PD)	14 (5.7)	20 (8.2)
Objective Radiological Response (CR + PR), n	88	73
Objective Radiological Response Rate, % (95% CI)	36.1 (30.0, 42.4)	30.0 (24.3, 36.2)

* Best Overall Response Rate refers to subjects with Overall Response Rate information

One Year Overall Survival Rate (ITT):

The overall survival rate at one year was 68.1% (95% CI 62.0 – 73.5) in participants treated with TTFields+GnP compared to 60.2% (95% CI 54.2 – 65.7) for participants treated with GnP alone..

Time to Pain Progression, Local Progression, or Death (ITT):

The median time to pain progression, local progression, or death was 9.1 months [95% CI: 7.4–10.2] in the TTFields+GnP arm and 7.5 months [95% CI: 6.5–8.5] in the GnP alone arm.

5*Puncture Free Survival:*

The median puncture-free survival time was 12.75 months [95% CI: 10.7–14.5] in the TTFields+GnP arm and 11.07 months [95% CI: 9.3–12.7] in the GnP alone arm.

Resectability Rate (ITT):

As shown in **Table 1**4, the resectability rate was 7.0% in the GnP Alone Arm and 10.1% in the Control Arm.

Table 14. Resectability Rate (ITT)

	TTFields + GnP (N=285)	GnP Alone (N=286)
Participants whose tumors were deemed resectable	20	29
Resectability rate, n (%)	7.0 (4.3, 10.6)	10.1 (6.9, 14.2)

Quality of Life:

Mean and median baseline QoL scores were comparable between the two arms for all scales/items. Median deterioration free survival (DFS) in health-related quality of life or death (defined as the time between randomization and first deterioration

in HRQoL score ≥ 10-point with no further improvement in HRQoL score ≥ 10 points), was estimated by Kaplan-Meier methodology using a two-sided stratified Cox Proportional Hazard model.

The addition of TTFields to GnP resulted in longer DFS in global health status, pain, pancreatic pain, and most of the digestive problems (**Figure 12**). Similar trends were observed for emotional function and fatigue/lack of energy.

Note, subjects who experienced local disease progression were not evaluated for QoL endpoints following progression. Consequently, these results do not capture the quality of life status of patients with local disease progression.

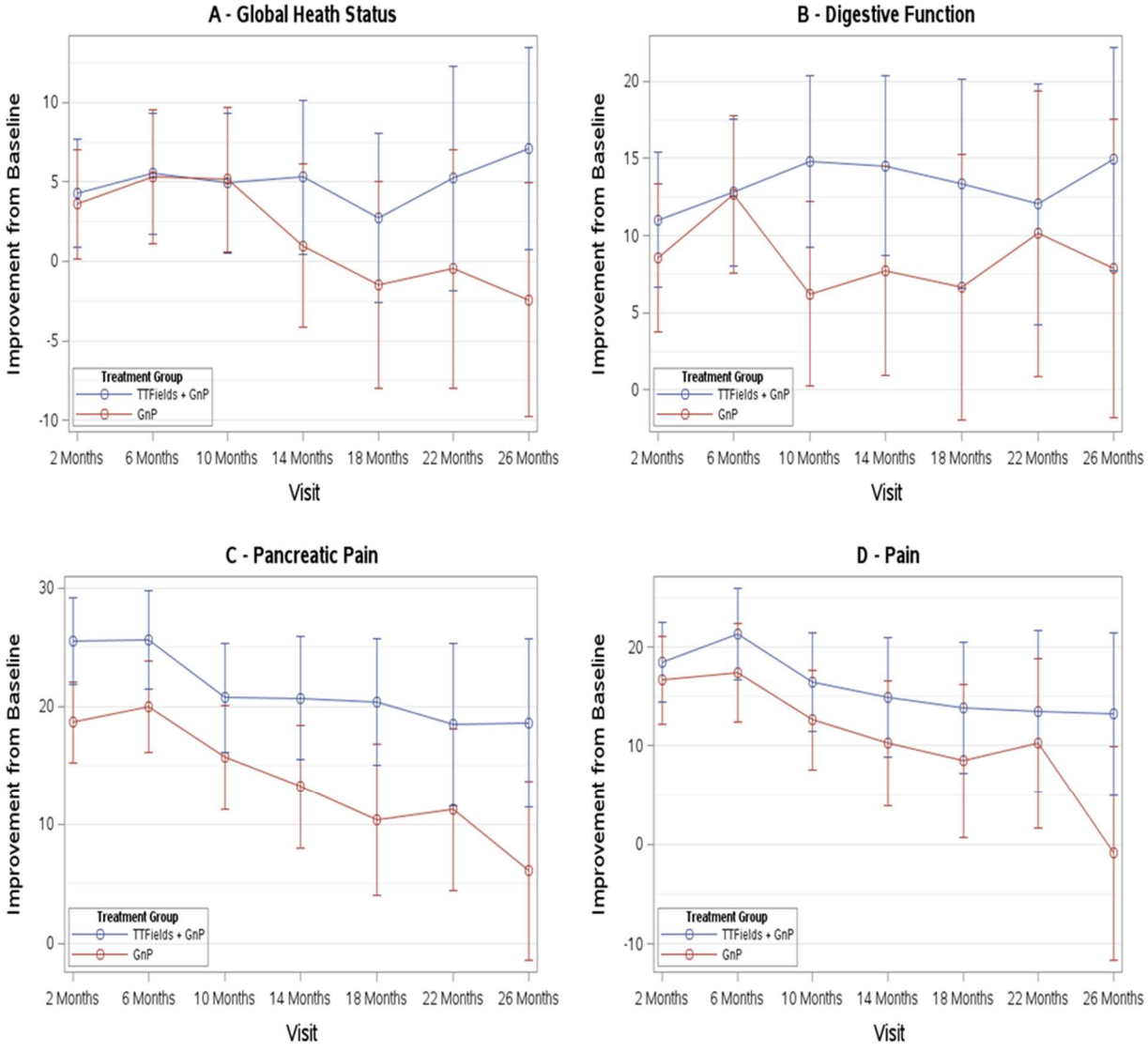


Figure 7. Improvement from Baseline Health-Related Quality of Life (ITT)

L. Safety Results

Overall, TTFields therapy was well-tolerated, with no exacerbation of GnP-related systemic toxicity, no new safety signals, and comparable Serious Adverse Event (SAE) between study arms. Most TTFields-treated patients experienced the expected device-related skin toxicity under the arrays (76.3% of the TTFields-treated participants). The majority of these events were low grade (Grade 1-2), with only 21 (7.7%) experiencing a Grade ≥3 event. The most common device-related Adverse Event (AE) not related to skin toxicity was fatigue, reported in 14 participants (5.1%). There was one Grade 4 AEs suspected to be related to the device by the investigator, which was a non-serious event of neutrophil count decrease. There were no device-related AEs that led to death, and no unanticipated device-related safety issues during the course of the study. The results have been summarized in Table 14 below.

Twenty one (21) patients in the TTFields + GnP group had grade ≥3 skin AEs. Median time to onset of first grade ≥3 skin and device-related AEs was 1.1 months (min, 0; max 16.6 months). Median time to resolution of the grade ≥3 skin and device-related AEs was 0.4 months (min, 0.1; max, 2.17 months).

Table 15. AEs by Severity, Per CTCAE Version 4.03 or Modified Grading for Skin AEs (Safety)

Severity	TTFields +GnP (N=274) n (%)	GnP Alone (N=273) n (%)	Overall (N=547) n (%)
Number of Subjects with at least one AE	268 (97.8)	270 (98.9)	538 (98.4)
Subjects with AE by Maximum CTCAE Grade			
Grade 1	4 (1.5)	4 (1.5)	8 (1.5)
Grade 2	21 (7.7)	36 (13.2)	57 (10.4)
Grade 3	164 (59.9)	151 (55.3)	315 (57.6)
Grade 4	62 (22.6)	63 (23.1)	125 (22.9)
Grade 5	17 (6.2)	16 (5.9)	33 (6.0)
Subjects with Study Device-related AE	222 (81.0)	NA	222 (40.6)
Subjects with Study Device-related AE by Maximum Severity			
Grade 1	79 (28.8)	NA	79 (14.4)
Grade 2	117 (42.7)	NA	117 (21.4)
Grade 3	25 (9.1)	NA	25 (4.6)
Grade 4	1 (0.4)	NA	1 (0.2)
Grade 5	0 (0)	NA	0 (0)
Subjects with Gemcitabine or Nab-paclitaxel related AE	258 (94.2)	263 (96.3)	521 (95.2)
Subjects with Gemcitabine or Nab-paclitaxel related AE by Maximum Severity			
Grade 1	4 (1.5)	11 (4.0)	15 (2.7)
Grade 2	50 (18.2)	61 (22.3)	111 (20.3)
Grade 3	155 (56.6)	142 (52.0)	297 (54.3)

Severity	TTFields +GnP (N=274) n (%)	GnP Alone (N=273) n (%)	Overall (N=547) n (%)
Grade 4	46 (16.8)	48 (17.6)	94 (17.2)
Grade 5	3 (1.1)	1 (0.4)	4 (0.7)
Device-related AE Leading to Device Discontinuation	23 (8.4)	NA	23 (4.2)
Systemic Therapy related AE Leading to Systemic Therapy Discontinuation	47 (17.2)	43 (15.8)	90 (16.5)
Subjects with SAE	147 (53.6)	131 (48.0)	278 (50.8)
Subjects with SAE by Maximum CTCAE Grade			
Grade 1	0 (0)	0 (0)	0 (0)
Grade 2	4 (1.5)	1 (0.4)	5 (0.9)
Grade 3	104 (38.0)	92 (33.7)	196 (35.8)
Grade 4	22 (8.0)	22 (8.1)	44 (8.0)
Grade 5	17 (6.2)	16 (5.9)	33 (6.0)
Subjects with Device related SAE	1 (0.4)	NA	1 (0.2)
Subjects with SAE related to Gemcitabine or Nab-paclitaxel	59 (21.5)	56 (20.5)	115 (21.0)
Subjects with SAE Leading to Death	17 (6.2)	16 (5.9)	33 (6.0)
Device-related SAE Leading to Death	0 (0)	NA	0 (0)
Systemic Therapy related SAE Leading to Death	3 (1.1)	1 (0.4)	4 (0.7)
Device-related SAE Leading to Device Discontinuation	0 (0)	NA	0 (0)
Systemic Therapy Related SAE Leading to Systemic Therapy Discontinuation	10 (3.6)	8 (2.9)	18 (3.3)

M. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

N. Pivotal Study Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 139 participating investigators, none of which were full-time or part-time employees of the sponsor. One of the investigators reported disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f). However, they did not hold a proprietary interest in the device, an equity interest in the Sponsor, or had entered into any arrangements with the Sponsor whereby the value of compensation could have been influenced by the outcome of the study. Details of the disclosable financial interests for the investigator, along with the steps taken to minimize the potential bias, were submitted in the PMA. The

applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND POST-PANEL ACTION

This PMA was not reviewed by an FDA Advisory Panel. A panel has previously reviewed the safety and effectiveness of the Applicant's technically similar TTFields device under P100034 that is indicated for the treatment of recurrent and newly diagnosed glioblastoma multiforme (GBM). In addition, the safety and effectiveness of the subject TTFields device has been approved by FDA under the original PMA (P230042) for the non-small cell lung cancer (NSCLC). This PMA does not raise any unanticipated safety or effectiveness issues that warrant submission to an Advisory Panel. In addition, the safety and probable benefit of the subject TTFields device has been approved by the FDA under H180002 for the treatment of malignant pleural mesothelioma.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The EF-27/PANOVA-3 trial met its primary endpoint, demonstrating that TTFields therapy added to GnP resulted in statistically significantly improvements in Overall Survival in patients with locally advanced pancreatic cancer compared to GnP alone (logrank test p = 0.039) The Hazard Ratio for OS was 0.82 (95% CI 0.68 – 0.99). The median OS in the TTFields+GnP arm was 16.2 months (95% CI 15.0-18.0) compared to 14.2 months (95% CI 12.8 – 15.4) in the GnP Alone arm.

The secondary endpoint of Progression free survival (PFS) was not met. The data does not show TTFields therapy added to GnP improves PFS compared with using GnP alone. Radiographic response rates were directionally aligned with the survival findings, increasing from 30.0% to 36.1% in the ITT population who had a CT scan after baseline.

B. Safety Conclusions

TTFields therapy was well-tolerated and with device-related skin toxicity events, predominantly mild to moderate, as the most common AE. No exacerbation of GnP-related systemic toxicity was reported, no exacerbation of GnP-related systemic toxicity was reported and no new safety signals emerged, and the rates of SAEs were comparable between study arms. The expected skin toxicity was reported in most participants, and 7.7% experienced grade ≥3 toxicity. There was one grade 4 device-related AE, and no device-related adverse events led to death.

Quality of Life metrics using the EORTC QLQ C-30 questionnaire and PAN26 module (Pancreatic Cancer) showed comparable QoL scores between the two arms

for all scales/items. The addition of TTFields+GnP resulted in longer deterioration free survival in global health status, pain, and pancreatic pain.

C. Benefit-Risk Conclusions

The results of the PANOVA-3 study demonstrate a favorable risk-benefit profile for TTFields therapy together with GnP in the treatment of locally advanced pancreatic cancer compared to GnP alone. TTFields therapy when used together with GnP in the PANOVA 3 study provided a clinically significant overall survival advantage compared to GnP alone. The extension in OS did not come at the expense of lower quality of life, or faster time to QoL deterioration.

Device related events were primarily localized skin reactions, usually low grade and manageable. Grade ≥3 events occurred in 7.7% of patients, and discontinuation due to device toxicity occurred in 2.6% of patients. No device related deaths or unanticipated device effects were reported, and the addition of TTFields did not increase systemic adverse events or alter the known safety profile of GnP.

The magnitude of benefit, coupled with the absence of added systemic toxicity and the manageable nature of device related risks, establish a favorable risk-benefit profile for TTFields therapy in this patient population with an unmet medical need.

1. Patient perspective

   The submission did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the treatment of adult patients with locally advanced pancreatic cancer, concomitant with gemcitabine and nab-paclitaxel, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. EF-27/PANOVA-3 trial met its primary endpoint. The addition of TTF to GnP alone resulted in statistically significant improvement in OS compared to GnP alone. Furthermore, improvements in patient-reported outcomes further support the demonstration of treatment effect.

Importantly, the addition of TTFields did not exacerbate the systemic toxicities of GnP. Adverse events were largely localized, predictable, and manageable, reinforcing the feasibility of adding TTFields therapy to current practice without compromising tolerability. Taken together, the totality of evidence supports

TTFields as a non-invasive therapy administered concomitantly with GnP, which offers the potential to improve overall survival and quality of life without introducing additional systemic toxicity.

XIII. CDRH DECISION

CDRH issued an approval order on February 11, 2026.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XIV. APPROVAL SPECIFICATIONS

A. Directions for Use:

See device labeling.

B. Hazards to Health from Use of the Device:

See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

C. Post-approval Requirements and Restrictions:

See Approval Order.