Phase 3 study of TTFields in locally advanced pancreatic adenocarcinoma (PANOVA-3): post-hoc subgroup analyses based on device usage and CA 19-9

2235P

Hani Babiker[1], Teresa Macarulla[2], Tomislav Dragovich[3], Philip Philip[4], Makoto Ueno[5], Eric Van Cutsem[6], Thomas Seufferlein[7], Vincent Picozzi[8], on behalf of the PANOVA-3 study investigators

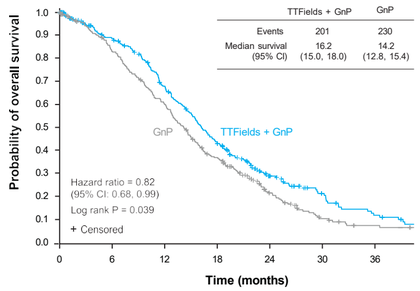
1. Mayo Clinic, Jacksonville, FL, USA; 2. Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; 3. Baptist MD Anderson Cancer Center, Jacksonville, FL, USA; 4. Wayne State University/Henry Ford Hospital, Detroit, MI, USA; 5. Kanagawa Cancer Center, Yokohama, Japan; 6. University Hospitals Gasthuisberg and University of Leuven (KUL), Leuven, Belgium; 7. University Hospital, Ulm, Germany; 8. Virginia Mason Medical Center, Seattle, WA, USA

Introduction

- Tumor Treating Fields (TTFields) are electric fields, delivered by a wearable device (**Figure 1**), that disrupt cancer cell division
- The PANOVA-3 trial (NCT03377491) demonstrated that TTFields plus gemcitabine/nab-paclitaxel (GnP) increased overall survival (OS) compared with GnP alone (16.2 vs 14.2 months; hazard ratio [HR] 0.82, p=0.039) in patients with unresectable locally advanced pancreatic adenocarcinoma (LA-PAC) (**Figure 2**)[1]
- The survival benefit observed with TTFields in PANOVA-3 was achieved with a median daily device usage of 62% (~15 h/day)
- OS in patients with PAC is known to be associated with carbohydrate antigen 19-9 (CA 19-9) pre-treatment levels and changes in levels over the course of therapy
- Post-hoc analyses of OS in patient subgroups in PANOVA-3 defined based on device usage, baseline CA 19-9 level, and changes over the course of therapy

Figure 1. NovoTTF-200T system used in PANOVA-3

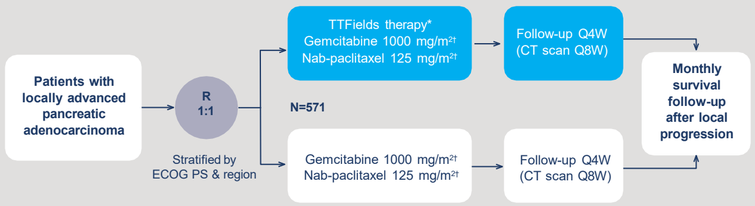
Figure 2. OS in the ITT population[2]



CI, confidence Interval; GnP, gemcitabine/nab-paclitaxel OS, overall survival; TTFields, Tumor Treating Fields.

Methods

Figure 3. PANOVA-3 study design (NCT03377491)[2]



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 medical device in torso
- Known allergies to medical adhesives, hydrogel, or chemotherapies

Primary endpoint:
- OS

Key secondary endpoints:
- PFS, ORR, QoL, resectability rate, safety, pain-free survival

*150 kHz, 18 h/day; †On days 1, 8, and 15 of each 28-day cycle.
CT, computerized tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; QoL, quality of life; Q4W, every 4 weeks; Q8W, every 8 weeks; R, randomization

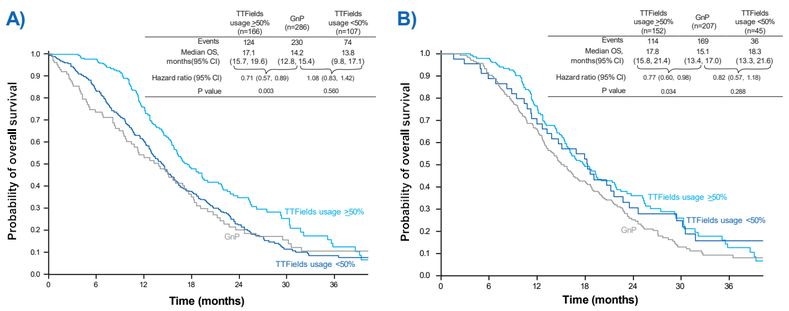
- Patients with previously untreated unresectable LA-PAC were randomized 1:1 to receive GnP with or without concomitant TTFields (**Figure 3**)
- Device usage time was assessed based on log files downloaded from the device
- Serum CA 19-9 levels were assessed at baseline and every 4 weeks until disease progression
- Exploratory post-hoc analyses of OS were performed based on;
  - Baseline CA 19-9 levels (Normal/Low <37 U/mL, Moderate 38–1,000 U/mL, High >1,000 U/mL, **Table 1**)
  - Change in CA 19-9 levels at week 8
  - Device usage during the first 3 months of therapy (≥50% and <50% average daily usage)
- OS for TTFields plus GnP and GnP alone was compared using a two-sided log-rank test
- Analyses were performed for the intent-to-treat population (ITT; all randomized patients) and the modified ITT population (mITT; patients who completed ≥1 28-day treatment cycle)

Results

Device usage

- In the ITT population
  - Average device usage ≥50% (≥12 hours/day) in the first 3 months of therapy was associated with significantly longer median OS with TTFields plus GnP (n=166) vs GnP alone (n=286): 17.1 vs 14.2 months, HR 0.71 [95% CI: 0.57, 0.89], p=0.003 (**Figure 3A**)
  - With average device usage <50% (n=107), median OS was not different between the two treatment arms: 13.8 months with TTFields plus GnP vs 14.2 months with GnP alone (HR 1.08 [95% CI: 0.83, 1.42], p=0.56) (**Figure 3A**)
- Similar results were observed for the mITT population
  - Average daily device usage ≥50% in the first 3 months was associated with significantly longer OS with TTFields plus GnP (n=152) vs GnP alone (n=207) (median 17.8 vs 15.1 months, HR 0.77 [95% CI: 0.60, 0.98], p=0.034) (**Figure 3B**)
  - With average device usage <50% (n=45), median OS was 18.3 months vs 15.1 months with GnP alone (HR 0.82 [95% CI: 0.57, 1.18], p=0.288) (**Figure 3B**)

Figure 3. OS of patients with device usage ≥50% in the first 3 months of therapy with TTFields plus GnP and GnP alone in A) the ITT and B) the mITT population



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

CA 19-9 levels

- Baseline CA 19-9 levels were high in a high proportion of patients and generally balanced between the treatment arms (**Table 1**)

Table 1. Baseline CA 19-9 levels in the ITT population

CA 19-9 level[1]	TTFields + GnP (N=285)	GnP alone (N=286)
Normal/low (≤37 U/mL), n (%)	48 (16.8)	44 (15.4)
Moderate (38–1,000 U/mL), n (%)	140 (49.1)	152 (53.1)
High/very high (>1,000 U/mL), n (%)	88 (30.9)	79 (27.6)
Untested, n (%)	9 (3.2)	11 (3.8)
Median (Q1–Q3)	411 (77–1,436)	345 (70–1,264)
Min–max	0–19,404	0.6–26,295

CA 19-9, carbohydrate antigen 19-9; GnP, gemcitabine/nab-paclitaxel; Min, minimum; Max, maximum; TTFields, Tumor Treating Fields

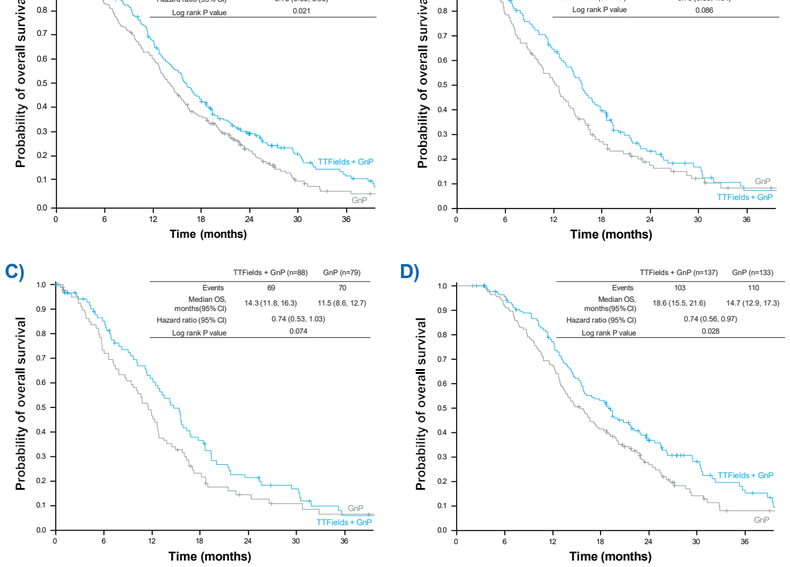
- Median OS was significantly longer for TTFields with GnP in patients with baseline CA 19-9 levels >37 U/mL and those with CA 19-9 decreases >50% at 8 weeks in both the ITT and mITT populations (**Table 2, Figure 4**)

Table 2. Median OS by baseline CA 19-9 levels and change in CA 19-9 levels at 8 weeks

CA 19-9 level[1]	Median OS, months (95% CI) TTFields + GnP	Median OS, months (95% CI) GnP alone	HR (95% CI), p value
ITT population			
Baseline >37 U/mL	16.1 (14.3, 18.0) (n=228)	14.1 (12.7, 15.4) (n=231)	0.78 (0.63, 0.96), p=0.021
Baseline >500 U/mL	15.4 (12.9, 17.1) (n=130)	12.1 (9.9, 13.8) (n=117)	0.78 (0.59, 1.04), p=0.086
Baseline >1000 U/mL	14.3 (11.8, 16.3) (n=88)	11.5 (8.6, 12.7) (n=79)	0.74 (0.53, 1.03), p=0.074
Decrease of >50% at 8 weeks	18.6 (15.5, 21.6) (n=137)	14.7 (12.9, 17.3) (n=133)	0.74 (0.56, 0.97), p=0.028
mITT population			
Baseline >37 U/mL	17.8 (15.5, 19.4) (n=161)	15.1 (13.2, 17.2) (n=167)	0.75 (0.59, 0.95), p=0.019
Baseline >500 U/mL	16.8 (14.7, 19.3) (n=88)	12.9 (10.8, 15.8) (n=88)	0.74 (0.53, 1.02), p=0.062
Baseline >1000 U/mL	15.8 (13.3, 18.6) (n=63)	12.7 (10.8, 16.3) (n=58)	0.75 (0.51, 1.10), p=0.144
Decrease of >50% at 8 weeks	19.2 (15.5, 21.8) (n=119)	14.7 (12.8, 17.3) (n=117)	0.71 (0.53, 0.95), p=0.019

CA 19-9, carbohydrate antigen 19-9; CI, confidence interval; GnP, gemcitabine/nab-paclitaxel; HR, hazard ratio; ITT, intent to treat; mITT, modified intent to treat; OS, overall survival; TTFields, Tumor Treating Fields.

Figure 4. OS in patients in the ITT population who had baseline CA 19-9 levels of A) >37 U/mL, B) >500 IU/mL, and C) >1,000 IU/mL and D) CA 19-9 decreases >50% at 8 weeks



CA 19-9, carbohydrate antigen 19-9; CI, confidence interval; GnP, gemcitabine/nab-paclitaxel; HR, hazard ratio; ITT, intent to treat; mITT, modified intent to treat; OS, overall survival; TTFields, Tumor Treating Fields

Discussion

- In this post-hoc analysis, an OS benefit was observed with the addition of TTFields therapy to GnP in patients who achieved a daily device usage of ≥50% during the first 3 months of therapy
- The survival benefit of TTFields therapy plus GnP (vs GnP alone) appears more pronounced in patients with baseline CA 19-9 levels >37 U/mL and patients who experienced a >50% decrease of CA 19-9 levels at 8 weeks of therapy
- Future analyses are needed to understand the effect of TTFields in medium/high CA 19-9 secreters

References

1. Babiker H, et al. J Clin Oncol 2025;43:2350–60; 2. Toms SA, et al. J Neurooncol 2019;141:467–73; 3. Leal T, et al. Lancet Oncol 2023;24:1002–17; 4.Kang Y-M, et al. Technol Cancer Res Treat 2021;20:15330338211043030.

Acknowledgements

PANOVA-3 was designed by Novocure GmbH and the investigators and was funded by Novocure GmbH. Medical writing assistance was provided by Andy Noble from Bioscript Group Ltd, Macclesfield, UK, and was funded by Novocure GmbH.

Disclosure

Hani Babiker: Consulting or Advisory Role: Endocyte, Celgene, Idera, Myovant Sciences, Novocure, Ipsen, Caris MPI, Incyte, Guardant Health; Speakers' Bureau: Guardant Health; Research Funding: Spirita Oncology, Novocure, AstraZeneca, JSI, Incyte, Qurient, HiFiBiO Therapeutics, Revolution Health Care, Elevation Oncology, Dragonfly Therapeutics, Zelbio, BMS, Mirati Therapeutics, Strategia (all research funding to Dr Babiker's institution).

Scan for a copy of this poster

Scan for more information on TTFields therapy