

# Long-term survival in patients with pancreatic cancer (PAC) treated with liposomal irinotecan in combination with 5-fluorouracil and leucovorin (nal-IRI+5-FU/LV)

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## INTRODUCTION

- Pancreatic cancer (PAC) is an aggressive disease with a poor prognosis; ~85% of patients are diagnosed at a locally advanced or metastatic (mPAC) stage
- Despite treatment, only 10% of patients with pancreatic cancer survive beyond 5 years
- Liposomal irinotecan in combination with 5-fluorouracil and leucovorin (nal-IRI+5-FU/LV) is the only approved second line (2L) therapy for mPAC following first line gemcitabine-based therapy
- The global, pivotal, phase 3 NAPOLI-1 trial reported a 1-year overall survival (OS) rate of 26% (95% confidence interval [CI]; 18–35%) in patients with mPAC treated with nal-IRI+5-FU/LV.<sup>1</sup> Factors associated with long-term survival ( $\geq 1$  year) in patients receiving nal-IRI+5-FU/LV were age  $\leq 65$  years, Karnofsky performance status (KPS)  $\geq 90$ , neutrophil-to-lymphocyte ratio (N/L)  $\leq 5$ , carbohydrate antigen (CA) 19-9  $< 59 \times$  the upper limit of normal, and no liver metastases
- The estimated probability of survival at 1 year in NAPOLI-1 is in line with the 1-year OS of 10–23% reported in a large European systematic review of observational studies that encompassed all mPAC stages and lines of therapy<sup>2</sup>
- Despite differences in baseline patient characteristics, a retrospective observational database study of >280 cancer clinics (699 patients) in the USA showed a similar 1-year OS rate of 29.1% (95% CI; 24.0–34.3) in those who received at least 4 treatment cycles of nal-IRI-based regimens.<sup>3</sup> One-year OS was lower (<20%) in patients treated with nal-IRI in later lines (>2L)
- In an attempt to predict long-term survival in patients treated with nal-IRI+5-FU/LV, a nomogram was derived from NAPOLI-1, which included: baseline KPS, albumin level, N/L, liver metastasis, CA19-9, disease stage at diagnosis, body mass index, and treatment arm (nal-IRI+5-FU/LV)<sup>4</sup>
- However, as illustrated by several published case studies, long-term survival can be achieved even when the patient has few of the positive prognostic characteristic listed above<sup>5–11</sup>
- Therefore, more data are needed on predictive factors of response to nal-IRI+5-FU/LV, which may better enable patient selection and improve survival outcomes



## AIM

- To evaluate survival outcomes and potential prognostic factors associated with long-term survival in real-world studies of patients with mPAC treated with nal-IRI+5-FU/LV following gemcitabine-based treatment



## METHOD

- This descriptive analysis includes real-world data from studies conducted in Korea, Italy and Germany, in patients with mPAC treated with 2L nal-IRI+5-FU/LV following gemcitabine-based therapy:

### Korean Pooled Analysis

- Pooled analysis (n=190) of two studies conducted by the Korean Cancer Study Group:
  - Retrospective, multicentre analysis (n=86); median age, 61 years; 61% male; Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0–1<sup>12</sup>
    - 59.4% of patients were treated with  $\geq 2$  prior lines of palliative chemotherapy
  - Retrospective, multicentre analysis (n=104); median age, 64 years; 59% male; ECOG PS 0–1 (82.7%), 2 (17.3%)<sup>13</sup>

### Italian Real-World Analysis

- Retrospective multicentre analysis (n=296); median age, 69 years; 51% male; ECOG PS 0 (44.0%), 1–2 (55.0%)<sup>14</sup>
- 25% of patients were treated with nal-IRI+5-FU/LV in third and fourth lines

### German iOMEDICO Registry

- Ongoing open, prospective, multicentre study (n=49); median age, 69 years; 45% male; ECOG PS 0 (8.2%), 1 (42.9%),  $\geq 2$  (14.3%).
- All patients are treated with 2L nal-IRI+5-FU/LV



## RESULTS

### Korean Pooled Analysis

- Median PFS and OS were 3.7 and 7.9 months, respectively
- OS rates for >10 months and >1 year were 14.2% and 6.3%, respectively
- The presence of liver metastasis was a negative predictive factor for survival >10 months (**Table 1**)

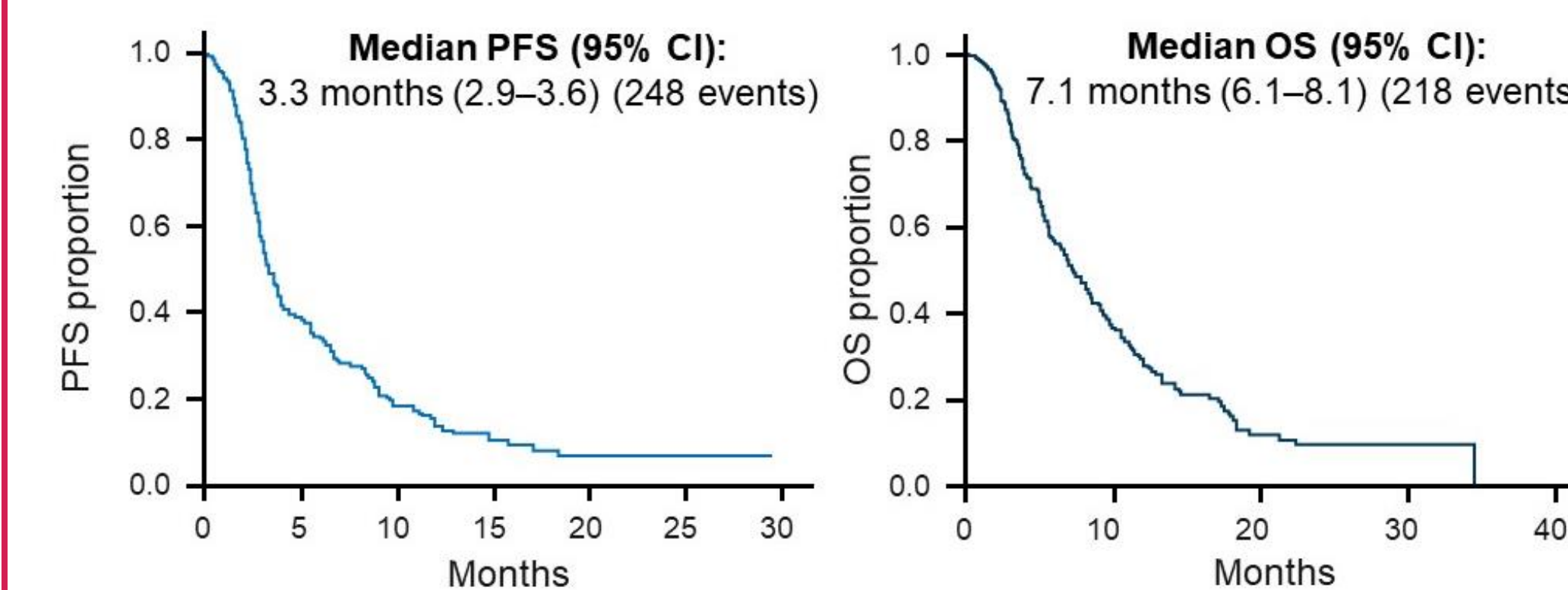
**Table 1.** Patient characteristics associated with >10 months survival<sup>a</sup>

Characteristic	OS <10 months (n=83)	OS >10 months (n=27)	
Age, years; <65/ $\geq 65$	55 (66.3%)/28 (33.7%)	13 (48.1%)/14 (51.9%)	$P=0.113$
Male/female	44 (53.0%)/39 (47.0%)	13 (48.1%)/14 (51.9%)	$P=0.825$
Prior surgery	14 (30.4%)	8 (44.4%)	$P=0.382$
<b>Liver metastases</b>	61 (73.5%)	12 (44.4%)	<b><math>P=0.009</math></b>
Lung metastases	16 (19.3%)	9 (33.3%)	$P=0.185$
Peritoneal metastases	33 (39.8%)	8 (29.6%)	$P=0.371$
CA 19-9 > 2 x ULN	50 (78.1%)	16 (66.7%)	$P=0.281$

<sup>a</sup>80 patients who survived at the time analysis and follow-up duration < 10 months were excluded in this analysis. CA, carbohydrate antigen; OS, overall survival; ULN, upper limit of normal

### Italian Real-World Analysis

**Figure 1.** Kaplan-Meier curves of survival outcomes following 2L nal-IRI+5-FU/LV



2L, second line; CI, confidence interval; OS, overall survival; PFS, progression-free survival

- Median PFS and OS were similar to results from NAPOLI-1 (**Figure 1**); the probabilities of OS for 6, 12 and 18 months were 53.4%, 18.0%, and 4.7%, respectively
- N/L ratio >5 was associated with a shorter OS, and albumin  $\geq 4$  g/dl was associated with a longer OS (**Table 2**)

### German Registry

- Of 49 patients followed-up to-date, 10 patients (20.4%) were long-term survivors ( $\geq 1$  year survival; **Table 3**)

**Table 3.** Survival outcomes following 2L nal-IRI+5-FU/LV: Analysis of long-term survivors ( $\geq 1$  year)

	PFS (n=10)	OS (n=10)
Events, n (%)	8 (80.0)	6 (60.0)
Median, months (95% CI)	11.6 (1.7–17.1)	16.6 (12.4–N/A)
6-months PFS rate (%)	66.7 (28.2–87.8)	-
12-months PFS rate (%)	44.4 (13.6–71.9)	-
18-months PFS rate (%)	11.1 (0.6–38.8)	-
6-months OS rate (%)	-	100.0
12-months OS rate (%)	-	100.0
18-months OS rate (%)	-	33.3 (6.3–64.6)

CI, confidence interval; N/A, not applicable; OS, overall survival; PFS, progression-free survival

**Table 2.** Characteristics associated with survival outcomes in multivariate analyses

Characteristics	Association with OS HR (95% CI), $P$ value
Baseline ECOG PS $\geq 1$	1.01 (0.71–1.45), $P=0.934$
CA19-9 >ULN <sup>a</sup>	1.14 (0.74–1.75), $P=0.553$
Number of metastatic sites >1	1.23 (0.88–1.71), $P=0.220$
<b>N/L ratio &gt;5</b>	<b>2.25 (1.50–3.39), <math>P=0.0001</math></b>
Haemoglobin $\geq 11$ g/dL	0.92 (0.64–1.33), $P=0.683$
<b>Albumin <math>\geq 4</math> g/dL</b>	<b>0.59 (0.38–0.91), <math>P=0.017</math></b>

<sup>a</sup>ULN defined as >37 ng/ml. CI, confidence interval; CA, carbohydrate antigen; ECOG PS, Eastern Cooperative Oncology Group PS; HR, hazard ratio; N/L, neutrophil-to-lymphocyte ratio; OS, overall survival; ULN, upper limit of normal

### Characteristics associated with survival following 2L nal-IRI+5-FU/LV

- There were no significant differences in tumour characteristics that might be of prognostic relevance for survival  $\geq 1$  year
- Factors that might be of prognostic relevance for long-term survival were:**
  - Patient characteristics
    - ECOG PS 0
    - Charlson Comorbidity Index 0
    - Age >65 years
  - Pre-treatment
    - Prior first-line gemcitabine-based combination therapy



## CONCLUSIONS

- Overall, this descriptive analysis of real-world data confirms the efficacy of nal-IRI+5-FU/LV in patients with mPAC that has progressed on a gemcitabine-based therapy**
- In the Korean, German and Italian studies, survival outcomes, including median PFS and OS rates, were similar to the NAPOLI-1 trial<sup>1</sup>**
- However the percentage of patients alive after 1 year is different in each of the retrospective studies, likely due to the heterogeneity of the population treated with nal-IRI/5-FU/LV (particularly the number of treatment lines received before nal-IRI/5-FU/LV)**
- Outcomes from the German Registry study assessed long-term and short-term survivors separately and data are not comparable; furthermore, these data are interim**
- Consistent with the NAPOLI-1–derived analyses<sup>1,4</sup>, presence of liver metastases was a negative predictor of long-term survival (Korean data), N/L ratio >5 was a negative predictor of long-term survival (Italian data), and albumin  $\geq 4$  g/dl was a positive predictor of long-term survival (Italian data)**
- Conversely, not all the items in the NAPOLI-1-derived analyses<sup>1,4</sup> were found to be predictors of long-term survival in these real-world settings, indicating the need for more data with defined lines of treatment received before nal-IRI/5-FU/LV**



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## CONTACT

A chart review on long-term survival of patients treated with nal-IRI+5-FU/LV will be started in 2023 in several countries. If centers are interested in participating in this project, they can contact SERVIER Medical Affairs Department or SERVIER local offices in their country.

Real-world one-year overall survival among patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) treated with liposomal irinotecan

