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Real-world efficacy and safety of liposomal irinotecan plus fluorouracil/leucovorin in patients with metastatic pancreatic adenocarcinoma: a study by the Korean Cancer Study Group

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Abstract

Background: Liposomal irinotecan (nal-IRI) plus 5-fluorouracil and leucovorin (5-FU/LV) was effective and well-tolerated in patients with metastatic pancreatic adenocarcinoma (mPAC) that progressed on gemcitabine-based therapy in the global NAPOLI-1 trial. Real-world data may further clarify the outcomes and safety profile of nal-IRI + 5-FU/LV in clinical practice.

Methods: This retrospective analysis included patients with mPAC who received nal-IRI + 5-FU/LV following gemcitabine-based therapy under a Managed Access Program in Korea.

Results: From January 2017 to April 2018, 86 patients across 10 institutions received nal-IRI + 5-FU/LV (median age, 61 years; 60% male; ECOG performance status, 0–1). A total of 35 (41%) and 51 (59%) patients had received less than two and two or more lines of chemotherapy before inclusion, respectively. At a median follow up of 6.4 months, median overall survival (OS) was 9.4 months (95% confidence interval [CI] 7.4–11.4) and median progression-free survival (PFS) was 3.5 months (95% CI 1.3–5.7). Six-month OS and PFS rates were 65.1% and 37.5%, respectively. Objective response and disease control rates were 10% and 55%, respectively. Most common grade 3–4 toxicities were neutropenia (37.2%), nausea (10.5%), vomiting (9.3%), anorexia (8.1%) and diarrhoea (4.7%).

Conclusion: Real-life data for Korean patients indicate that, consistent with NAPOLI-1, nal-IRI + 5-FU/LV is effective and well-tolerated in patients with mPAC that progressed on gemcitabine-based therapy.

Keywords: chemotherapy, liposomal irinotecan, pancreatic adenocarcinoma, real-world evidence

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Introduction

Pancreatic adenocarcinoma (PAC) is an aggressive disease with a dismal prognosis, which is mainly associated with its detection at an advanced stage and frequent recurrence even after curative resection. Fewer than 10% of patients survive at 5 years after diagnosis.[1,2]

Gemcitabine has been the standard therapy for unresectable or metastatic PAC (mPAC) for the past two decades.[3] The development of two combination chemotherapeutic regimens, FOLFIRINOX [oxaliplatin, irinotecan, fluorouracil (5-FU) and leucovorin (LV)] and gemcitabine plus *nab*-paclitaxel, has significantly improved patient outcomes

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as front-line chemotherapy.[4,5] These regimens delay the deterioration of quality of life for patients with mPAC, improving the chance for salvage chemotherapy after progression on first-line chemotherapy.[6–8]

Few phase III trials have addressed the role of salvage chemotherapy after failure of first-line chemotherapy. Although the addition of oxaliplatin to 5-FU/LV improved survival outcomes compared with 5-FU/LV in patients showing disease progression on gemcitabine in the previous CONKO-003 trial,[9] this finding was not reproduced in the PANCREOX study, in which oxaliplatin was combined with 5-FU/LV infusion.[10] The role of oxaliplatin in the management of patients with mPAC that progressed on first-line gemcitabine-based therapy is therefore controversial.

Liposomal irinotecan (nal-IRI) consists of irinotecan sucrosofate salt encapsulated in liposome particles, which increase and prolong the intratumoural levels of both irinotecan and its active metabolite SN-38.[11] The promising activity of nal-IRI against PAC in a phase II trial[12] led to the design of the pivotal phase III NAPOLI-1 trial, in which nal-IRI + 5-FU/LV showed higher effectiveness than 5-FU/LV alone and manageable toxicities in patients with mPAC following previous gemcitabine-based therapy.[13] In the NAPOLI-trial, nal-IRI + 5-FU/LV was used as first-line (13%), second-line (53%) and third-line or later (34%) chemotherapy for the management of metastatic disease.

Although 30% of patients in the NAPOLI-1 trial were of East Asian ethnicity, including patients from Korea,[13] FOLFIRINOX or gemcitabine plus *nab*-paclitaxel were not widely used at the time of the study. These modern front-line regimens are now commonly used after their approval for reimbursement by the Korean National Healthcare Insurance in 2016. Considering the effect of the changes in front-line chemotherapy on the effectiveness of salvage therapy and the heterogeneity of clinical features and management of mPAC, real-world data are needed for nal-IRI + 5-FU/LV treatment.

The present multicentre, retrospective, observational study was conducted by the Korean Cancer Study Group (KCSG) to evaluate the effectiveness and safety of nal-IRI + 5-FU/LV in patients with mPAC following disease progression on previous gemcitabine-based therapy.

Methods

Patients

This retrospective study was a multicentre, open-label, non-comparative observational study that included patients who entered into the nal-IRI Managed Access Program (MAP) in Korea. This analysis was performed by the hepatobiliary and pancreatic cancer division of the KCSG. Effectiveness and safety data were retrospectively collected and analysed and the study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the institutional review board (IRB) at the main study site (Asan Medical Center, approval number 2018-0492), with additional local approvals granted at other study sites as required. At 3 of the 10 participating institutions in this study (Dong-A University Hospital, Bucheon St. Mary's Hospital and Korea University Hospital), additional approval was waived according to local IRB policy (additional local approval not required in the case of multicentre, retrospective analyses). Approval numbers from the remaining six institutions were as follows: Cha University Hospital (2018-07-008-001); Dongguk University Hospital (110757-201808-HR-02-03); Haeundae Baik Hospital (2018-04-009-005); Seoul National University Hospital (1809-012-969); Samsung Medical Center (2018-03-162); and Yonsei University College of Medicine (Severance Hospital; 4-2017-1011). IRBs waived the need for informed consent for this study owing to the nonrequirement of consent in retrospective analysis covered by regulations in Korea.

Patients with histologically or cytologically confirmed mPAC were eligible for inclusion in this MAP if they had evidence of disease progression on prior gemcitabine-based therapy, including neoadjuvant, adjuvant or palliative chemotherapy. All patients who had previously received conventional irinotecan as part of a FOLFIRINOX regimen had progressed prior to administration of nal-IRI during the MAP.

Patients received nal-IRI + 5-FU/LV as described in the NAPOLI-1 trial (80 mg/m^2 irinotecan hydrochloride trihydrate salt equivalent to 70 mg/m^2 irinotecan free base over 90 min, followed by 400 mg/m^2 LV over 30 min and then 2400 mg/m^2 5-FU over 46 h, every 2 weeks). Computed tomography scans were performed every 6–8 weeks.

Adverse events were evaluated during every clinic visit and graded according to the National Cancer

Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.03. Effectiveness was measured using radiological assessments, including computed tomography or magnetic resonance imaging scans, and graded according to the Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1.

Statistical analysis

The objective response rate (ORR) and disease control rate (DCR) were assessed using RECIST v1.1. Progression-free survival (PFS) was defined as the time from the initiation of nal-IRI + 5-FU/LV to the date of disease progression determined by RECIST v1.1 or death, whichever occurred first. Overall survival (OS) was defined as the time between the initiation of nal-IRI + 5-FU/LV and death from any cause. Survival outcomes were estimated using Kaplan–Meier curves and subgroups compared using the log-rank test. Univariate and multivariate analyses of OS and PFS were performed using the Cox proportional hazards model. A two-sided p value <0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (IBM, Armonk, NY, USA) version 22.0.

Results

Baseline characteristics

The MAP enrolled 86 patients with mPAC from ten Korean institutions between January 2017 and April 2018. Baseline patient characteristics are summarised in Table 1. Median age was 61 years (range, 37–79) and 52 patients (60.5%) were male. Most patients had a primary tumour in the pancreatic head ($n=41$, 47.7%) followed by the tail ($n=27$, 31.4%) and body ($n=17$, 19.8%). All patients had metastatic disease and Eastern Cooperative Oncology Group performance status 0–1 at the time of nal-IRI + 5-FU/LV initiation. The most common metastatic sites were the liver ($n=49$, 57.0%), peritoneum ($n=30$, 34.9%) and lung ($n=27$, 31.4%). Serum CA 19-9 levels were elevated in 59 (83.1%) of 71 patients with available data at initiation of nal-IRI + 5-FU/LV treatment.

Curative surgery and chemoradiotherapy were previously performed in 39 (45.3%) and 20 (23.3%) patients, respectively. A median of two lines (range, 1–4) of chemotherapy (including neoadjuvant, adjuvant and palliative therapy) were given prior to nal-IRI + 5-FU/LV treatment. The median number of lines for palliative therapy only for locally advanced or mPAC was also two (range, 0–4). Irinotecan was previously administered as a component of FOLFIRINOX in 18 patients (20.9%). This was received as neoadjuvant therapy in two of these patients, and disease progression was observed in all patients who had previously been treated with irinotecan. Gemcitabine plus *nab*-paclitaxel and 5-FU/LV were previously administered in 51 (59.3%) and 59 patients (68.6%), respectively.

Effectiveness outcomes

Effectiveness outcomes with nal-IRI + 5-FU/LV are summarised in Table 2. The median follow-up duration was 6.4 months (95% confidence interval [CI] 5.5–7.3 months), median OS was 9.4 months (95% CI 7.4–11.4 months) and median PFS was 3.5 months (95% CI 1.3–5.7 months). Six-month OS and PFS rates were 65.1% (95% CI 53.8–74.3%) and 37.5% (95% CI 27.1–47.8%), respectively (Figure 1). Median OS since the start of first-line therapy for unresectable or metastatic disease was 26.3 months (95% CI 19.3–33.5 months) and the 2-year OS rate was 54.3%.

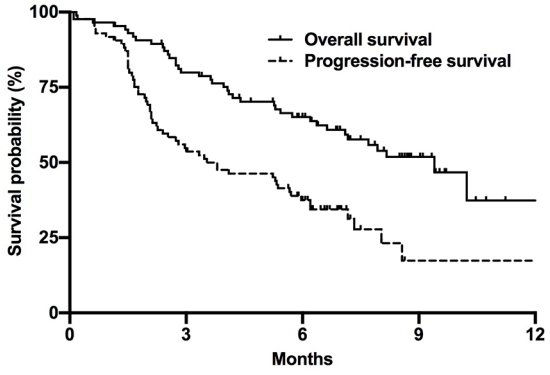

Figure 1. Survival outcomes with nal-IRI + 5-FU/LV.

According to RECIST v1.1, complete response (CR) and partial response (PR) were achieved in two (2.3%) and seven (8.1%) patients, respectively, indicating an ORR of 10.5% (95% CI 3.9–17.1%). Stable disease (SD) and progressive disease (PD) were the best response in 38 (44.2%) and 32 (37.2%) patients, respectively, and response evaluation was not available in seven patients (8.1%). The DCR was 54.7% (95% CI 36.1–58.1%).

Table 1. Patient characteristics.

Variable	nal-IRI + 5-FU/LV (*n* = 86)
Gender	
Male	52 (60.5%)
Female	34 (39.5%)
Age, median (range)	61 (37–79)
<65	55 (64.0%)
⩾65	31 (36.0%)
Primary tumour site	
Head	41 (47.7%)
Body	17 (19.8%)
Tail	27 (31.4%)
Multi-centric	1 (1.2%)
Site of metastasis	
Liver	49 (57.0%)
Lung	27 (31.4%)
Bone	4 (4.7%)
Peritoneum	30 (34.9%)
Lymph node	21 (24.4%)
Other	15 (17.4%)
Baseline CA 19-9 level (U/ml), median (range)	844 (1.2–124,073)
⩽1 × UNL	12 (14.0%)
>1 and ⩽2 × UNL	4 (4.7%)
>2 × UNL	55 (64.0%)
N/A	15 (17.4%)
Prior surgical resection	39 (45.3%)
Prior concurrent chemoradiotherapy	20 (23.3%)
Prior lines of palliative chemotherapy, median (range)	2 (0–4)
0	8 (9.3%)
1	27 (31.4%)
2	36 (41.9%)
3	12 (14.0%)
4	3 (3.5%)
Prior first-line palliative chemotherapy	*n* = 78
Gemcitabine monotherapy	12 (14.0%)
Gemcitabine plus *nab*-paclitaxel	44 (51.2%)
FOLFIRINOX	14 (16.3%)
Others	8 (9.3%)
Prior irinotecan-containing chemotherapy (FOLFIRINOX)	18 (20.9%)
Prior gemcitabine plus *nab*-paclitaxel chemotherapy	51 (59.3%)
Prior 5-FU/LV containing chemotherapy	59 (68.6%)

CA 19-9, carbohydrate antigen 19-9; UNL, upper normal limit; N/A, not available.

Among 51 patients with available pre- and post-treatment CA 19-9 levels, 16 (31.4%) achieved a CA 19-9 response (i.e. a ⩾50% decrease in CA 19-9 levels from baseline).[13]

Survival outcomes by prior chemotherapy

Survival outcomes with nal-IRI + 5-FU/LV were analysed by the number of lines of prior chemotherapy in the palliative setting (Figure 2A and B) and prior first-line chemotherapy regimen (Figure 2C and D). Median OS and PFS did not differ significantly according to the number of lines of previous palliative chemotherapy (<2 *versus* ⩾2) ($p = 0.64$ and $p = 0.09$, respectively). Median OS was 7.9 months (95% CI not available) in patients who received ⩾2 lines ($n = 51$) of palliative chemotherapy, and was not reached at the time of analysis in patients who received <2 lines ($n = 35$) of treatment. Median PFS in these groups was 6.0 months (95% CI 3.3–8.6 months) and 3.0 months (95% CI 1.6–4.4 months) in patients who received <2 lines and ⩾2 lines of palliative chemotherapy, respectively. Six-month OS rate was 68.3% (95% CI 50.1–81.0%) in patients who had received <2 lines of palliative chemotherapy, and 62.8% (95% CI 47.5–74.7%) in those who had received ⩾2 lines of palliative chemotherapy. Six-month PFS rate was 48.6% (95% CI 30.8–64.4%) in patients who had received <2 lines of palliative chemotherapy, and 30.0% (95% CI 18.0–42.9%) in those who had received ⩾2 lines of palliative chemotherapy.

The median OS with nal-IRI + 5-FU/LV did not differ significantly according to the first-line palliative chemotherapy regimen ($p = 0.31$, Figure 2C), whereas the difference in PFS was significant ($p = 0.02$, Figure 2D). The median PFS with nal-IRI + 5-FU/LV was 18.0 months (95% CI not available), 3.5 months (95% CI 0.9–6.2 months), and 1.7 months (95% CI 1.3–2.1 months) in patients who previously received first-line gemcitabine ($n = 12$), gemcitabine plus *nab*-paclitaxel ($n = 44$), and FOLFIRINOX ($n = 14$), respectively. Median OS was 10.2 months in patients who had not previously received irinotecan; and 4.4 months in patients who had received and progressed on prior neoadjuvant or palliative irinotecan treatment ($n = 18$; $p = 0.011$). Median PFS was 4.4 months in patients who had not previously received irinotecan; and 1.7 months in patients who had received and progressed on prior neoadjuvant or palliative irinotecan treatment ($p < 0.001$).

Table 2. Effectiveness outcomes.

	nal-IRI + 5-FU/LV ($n = 86$)
Best response	
CR	2 (2.3%)
PR	7 (8.1%)
SD	38 (44.2%)
PD	32 (37.2%)
N/A	7 (8.1%)
6-month OS, % (95% CI)	65.1 (53.8–74.3)
Median OS, months (95% CI)	9.4 (7.4–11.4)
6-month PFS, % (95% CI)	37.5 (27.1–47.8)
Median PFS, months (95% CI)	3.5 (1.3–5.7)
Objective response rates (CR + PR)	9 (10.5%)
Disease control rate (CR + PR + SD)	47 (54.7%)

CI, confidence interval; CR, complete response; N/A, not available; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Multivariate analysis of prognostic factors

In the multivariate analyses of survival outcomes (Table 3: OS and PFS), bone metastases (HR, 8.28; 95% CI 2.06–33.33; $p = 0.003$) were significantly associated with worse OS outcomes; and age (< *versus* ⩾65 years: HR, 0.39; 95% CI 0.20–0.78; $p = 0.007$), liver metastases (HR, 2.96; 95% CI 1.46–6.02; $p = 0.003$), bone metastases (HR, 7.47; 95% CI 2.12–26.28; $p = 0.002$), and previous first-line FOLFIRINOX (*versus* gemcitabine monotherapy: HR, 4.08; 95% CI 1.21–13.73; $p = 0.02$) were significantly associated with worse PFS outcomes.

Safety profile

Adverse events that occurred in >10% of patients are listed in Table 4. Any-grade adverse events were observed in the majority of patients ($n = 78$, 90.7%), and severe grade 3–4 toxicities were observed in 49 patients (57.0%). There was no treatment-related mortality. The most common adverse events were neutropenia ($n = 45$, 52.3%), anaemia ($n = 44$, 51.2%), nausea ($n = 40$, 46.5%), anorexia ($n = 32$, 37.2%), and diarrhoea ($n = 26$, 30.2%). Grade 3–4 neutropenia ($n = 32$, 37.2%),

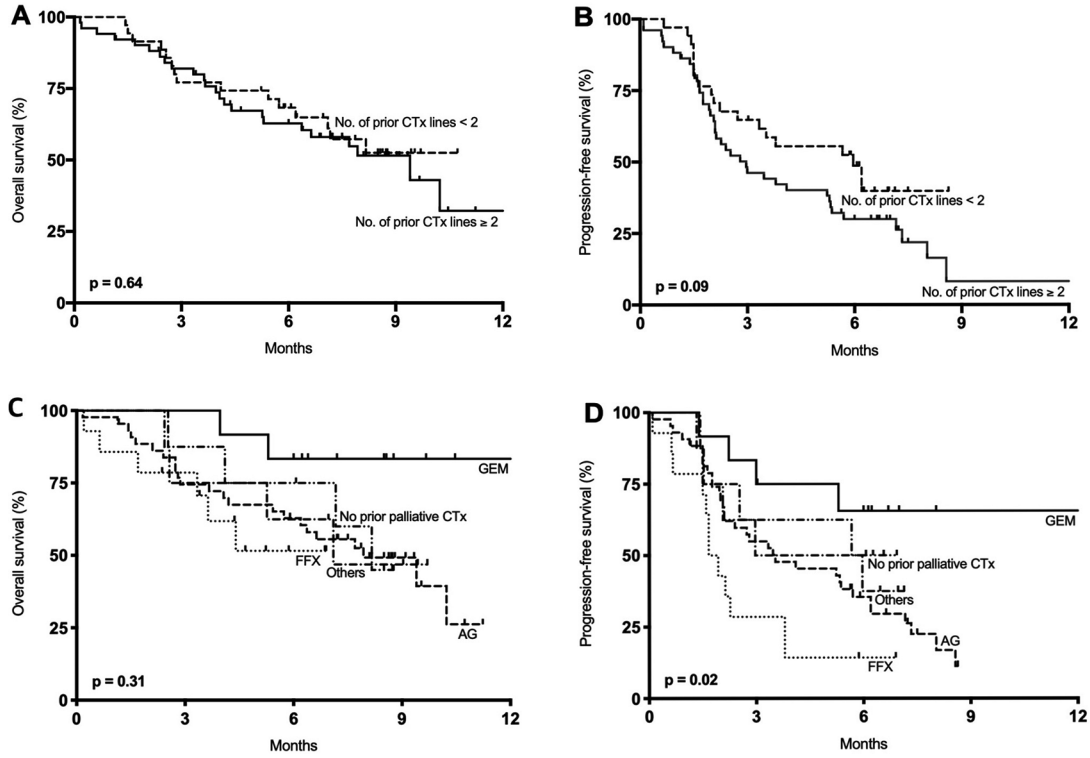

Figure 2. Survival outcomes with nal-IRI + 5-FU/LV according to number of previous lines of palliative chemotherapy and type of first-line therapy: (A) overall survival according to number of previous lines of palliative chemotherapy; (B) progression-free survival according to number of previous lines of palliative chemotherapy; (C) overall survival according to type of first-line palliative chemotherapy; and (D) progression-free survival according to type of first-line palliative chemotherapy.
AG, gemcitabine plus nab-paclitaxel; CTx, chemotherapy; FFX, FOLFIRINOX; GEM, gemcitabine monotherapy.

nausea ($n = 9$, 10.5%), vomiting ($n = 8$, 9.3%) and diarrhoea ($n = 4$, 4.7%) were the most frequent severe toxicities reported. Febrile neutropenia occurred in seven patients (8%).

Treatment exposure and dose modification

The median treatment duration of nal-IRI + 5-FU/LV was 3.1 months (range, 0.5–16.7). At the time of this analysis, nal-IRI + 5-FU/LV was ongoing in 18 patients (20.9%). Treatment was discontinued because of disease progression in 45 patients (66.2%) and adverse events in 8 (11.8%). The adverse events were grade 3 fatigue ($n = 2$), grade 3 diarrhoea ($n = 2$), grade 3 anorexia ($n = 1$), grade 3 febrile neutropenia ($n = 1$), grade 3 pneumonia ($n = 1$) and grade 4 neutropenia ($n = 1$). nal-IRI + 5-FU/LV doses were reduced or delayed in 43 patients (50.0%). The most frequent reasons for dose modification of nal-IRI + 5-FU/LV were neutropenia ($n = 20$, 23.3%), fatigue ($n = 10$, 11.6%) and nausea/vomiting ($n = 5$, 5.8%). Diarrhoea was a reason for dose modification in only 2 (4.7%) patients. Subsequent chemotherapy was administered to 15 patients (22.1%) following failure of nal-IRI + 5-FU/LV.

Discussion

The present multicentre retrospective study is one of the largest real-world analyses of nal-IRI + 5-FU/LV since modern front-line chemotherapy regimens such as FOLFIRINOX and gemcitabine plus *nab*-paclitaxel became available.

In the current study, the 6-month OS rate was 65.1%, and the median OS was 9.4 months. nal-IRI + 5-FU/LV resulted in a median PFS of 3.5 months and an ORR of 10.5%. These findings were consistent with the results of the NAPOLI-1 study and previous retrospective analyses,[13,14] particularly with the Asian subgroup analysis.[15] In the NAPOLI-1 study, the median OS and PFS were 6.1 and 3.1 months, respectively, and the ORR was 16% in the nal-IRI + 5-FU/LV group.[13] In a

Table 3. Multivariate analyses of survival outcomes.

	Progression-free survival			Overall survival		
	HR	**95% CI**	***p* value**	**HR**	**95% CI**	***p* value**
Sex (female *versus* male)	1.21	0.67–2.18	0.538	0.90	0.45–1.81	0.772
Age (⩾65 *versus* <65 years)	0.39	0.20–0.78	**0.007**	0.83	0.39–1.77	0.627
Liver metastases	2.96	1.46–6.02	**0.003**	–	–	–
Bone metastases	7.47	2.12–26.28	**0.002**	8.28	2.06–33.33	**0.003**
Peritoneum metastases	–	–	–	1.89	0.93–3.87	0.080
Prior surgical resection	1.50	0.82–2.73	0.184	–	–	–
Prior lines of palliative chemotherapy (⩾2)	0.62	0.27–1.40	0.247	1.43	0.63–3.24	0.389
Prior first-line palliative chemotherapy						
Gemcitabine monotherapy	Ref	–	0.100	Ref	–	0.458
Gemcitabine plus *nab*-paclitaxel	2.55	0.89–7.34	0.082	4.08	0.95–17.50	0.059
FOLFIRINOX	4.08	1.21–13.73	**0.023**	4.10	0.78–21.56	0.095
Others	2.69	0.65–11.10	0.172	3.66	0.63–21.33	0.149
No previous palliative chemotherapy	0.85	0.18–3.92	0.836	3.92	0.60–25.50	0.153

CI, confidence interval; HR, hazard ratio; Ref, reference.

recent retrospective analysis of nal-IRI + 5-FU/LV, the median OS and PFS were 5.3 and 2.9 months, respectively, and the ORR was 5%.[14] The consistent clinical outcomes of these studies, despite variation in baseline patient characteristics, support the clinical relevance of nal-IRI + 5-FU/LV in patients with mPAC that progressed following prior gemcitabine-based therapy.

Improved effectiveness of first-line chemotherapy has led to an increase in the number of patients treated with salvage therapy for unresectable or metastatic disease. In the current study population, the median OS from the start of first-line palliative chemotherapy for unresectable or metastatic disease was 26.3 months. Although this analysis included patients with good performance status and organ function who were eligible for subsequent chemotherapy following disease progression on prior therapies, the findings support the notion that long-term survival may be achieved using appropriate sequential chemotherapy in the subset of patients with mPAC. This underscores the importance of selecting optimal chemotherapy regimens after progression on first-line chemotherapy. A reduced OS effect with nal-IRI + 5-FU/LV in patients who previously received and progressed on conventional irinotecan has already been reported.[13,14] In the current study, survival outcomes were poorer in patients who had previously received conventional irinotecan. Discrepancy in the survival outcomes with nal-IRI + 5-FU/LV according to the prior exposure and progression to conventional irinotecan in the studies might be caused by the development of resistance to irinotecan or SN-38 (active metabolite of irinotecan) during prior treatment using conventional irinotecan. Although nal-IRI modifies the pharmacological properties of irinotecan, resulting in greater exposure of irinotecan and SN-38, this might be insufficient to overcome the resistance to this molecule. However, the number of patients in this group in the studies including ours was small, and thus further evaluation is needed.

The safety profile of nal-IRI + 5-FU/LV reported in this real-world study was consistent with the results of the NAPOLI-1 trial and its associated Asian subgroup analysis.[13,15] The most common grade 3–4 toxicities were neutropenia, nausea, vomiting, anaemia and diarrhoea. Febrile

Table 4. Adverse events occurring in >10% of patients for any grade.

Preferred terms (PT)	Any grade	Grade 3–4
All, *n* (%)	78 (90.7%)	49 (57.0%)
Neutropenia, *n* (%)	45 (52.3%)	32 (37.2%)
Anaemia, *n* (%)	44 (51.2%)	7 (8.1%)
Alopecia, *n* (%)	16 (18.6%)	NA
Fatigue, *n* (%)	25 (29.1%)	2 (2.3%)
Anorexia, *n* (%)	32 (37.2%)	7 (8.1%)
Nausea, *n* (%)	40 (46.5%)	9 (10.5%)
Vomiting, *n* (%)	28 (32.6%)	8 (9.3%)
Diarrhoea, *n* (%)	26 (30.2%)	4 (4.7%)

n = 86; NA, not applicable.

neutropenia occurred in seven patients. The incidence of non-haematological toxicities such as diarrhoea was lower than reported in the intention-to treat population of the NAPOLI-1 trial. This might be explained by potential ethnic differences in pharmacokinetics and pharmacogenomics governing the metabolism of nal-IRI, or toxicities may have been underestimated owing to the retrospective nature of this analysis.[16]

The effectiveness of nal-IRI + 5-FU/LV demonstrated in this study and the NAPOLI-1 Asian subgroup analysis has important clinical implications for the future investigation of nal-IRI-containing regimens. These include neoadjuvant and adjuvant chemotherapy for potentially curative surgery or front-line chemotherapy for unresectable or metastatic disease. Future trials of nal-IRI with oral 5-FU to reduce infusion time may also be clinically relevant in terms of patient convenience.

The present study had several limitations. It was retrospective, which may result in potential selection or recall bias. Moreover, nal-IRI + 5-FU/LV was administered as several lines of chemotherapy following progression on gemcitabine-containing regimens. Some caution is therefore warranted in the interpretation of these results. This program did not include any patients with ECOG performance status >2, although this is likely due to physician concern over the potential for toxicities in patients with poorer performance status, reflecting clinical practice. Moreover, our findings were based on an ethnically homogeneous population as all patients were of East Asian origin and were from South Korea. The advantages of this study include its use of extensive real-world data gathered from multiple centres, and that patient characteristics were similar to those observed in the NAPOLI-1 trial, allowing balanced comparisons to be made between the two studies.

In conclusion, this multicentre, retrospective, observational study demonstrated that the effectiveness and safety of nal-IRI + 5-FU/LV in clinical practice was similar to that observed in NAPOLI-1, particularly to the results observed in Asian patients who were enrolled in that study.[13,15] The results presented here show that nal-IRI + 5-FU/LV was an effective and feasible therapy in patients with mPAC after failure of gemcitabine-based therapy in a real-world clinical setting. nal-IRI + 5-FU/LV is a clinically relevant and valuable addition to the arsenal of treatments for mPAC, characterised by a high unmet need, exemplified by limited survival and lack of treatment options. Future investigation of nal-IRI and optimal sequence of chemotherapy is warranted to improve clinical outcomes of patients with PAC across different clinical settings.

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Conflict of interest statement

CY has received research funding from Shire and Servier, and has acted as an advisor for Shire.

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