Liposomal Irinotecan + 5-Fluorouracil/Leucovorin in Metastatic Pancreatic Cancer

Subgroup Analyses of Patient, Tumor, and Previous Treatment Characteristics in the Pivotal NAPOLI-1 Trial

SUPPLEMENTAL DIGITAL CONTENT

SUPPLEMENTAL TABLE 1. Baseline Characteristics for the nal-IRI+5-FU/LV and 5-FU/LV Arms in the NAPOLI-1 ITT Population

	Overall Population		
	ITT (N = 417)	**nal-IRI+5-FU/LV (n = 117)**	**5-FU/LV (n = 119)**
Sex, n (%)			
Female	180 (43)	48 (41)	52 (44)
Male	237 (57)	69 (59)	67 (56)
Age, median (IQR) (range), y	63 (57–70) (31–87)	63 (57–70) (41–81)	62 (55–69) (34–80)
Previous lines of metastatic therapy, n (%)			
0	51 (12)	15 (13)	15 (13)
1	234 (56)	62 (53)	67 (56)
≥2	132 (32)	40 (34)	37 (31)
KPS score, n (%)			
90–100	231(55)	69 (59)	57 (48)
70–80	182 (44)	45 (38)	61 (51)
50–60	3 (1)	3 (3)	0
Missing	1 (0.2)	0	1 (1)
Primary tumour location, n (%)			
Head	256 (61)	76 (65)	69 (58)
Other	161 (39)	41 (35)	50 (42)
Measurable metastatic lesions at baseline, n (%)			
1	81 (19)	19 (16)	22 (19)
2	184 (44)	49 (42)	58 (49)
3	65 (16)	22 (19)	15 (13)
>3	24 (6)	7 (6)	8 (7)
Liver metastases, n (%)	284 (68)	75 (64)	83 (70)
CA 19-9, median (IQR), U/mL	1542 (120–12815)	127 (120–9001)	1292 (99–16381)
Albumin, median, g/dL	4.0	4.1	4.0

IQR indicates interquartile range; ITT, intent-to-treat; KPS, Karnofsky performance status.

SUPPLEMENTAL TABLE 2. Efficacy Outcomes by Number of Metastatic Lesions in the NAPOLI-1 ITT Population

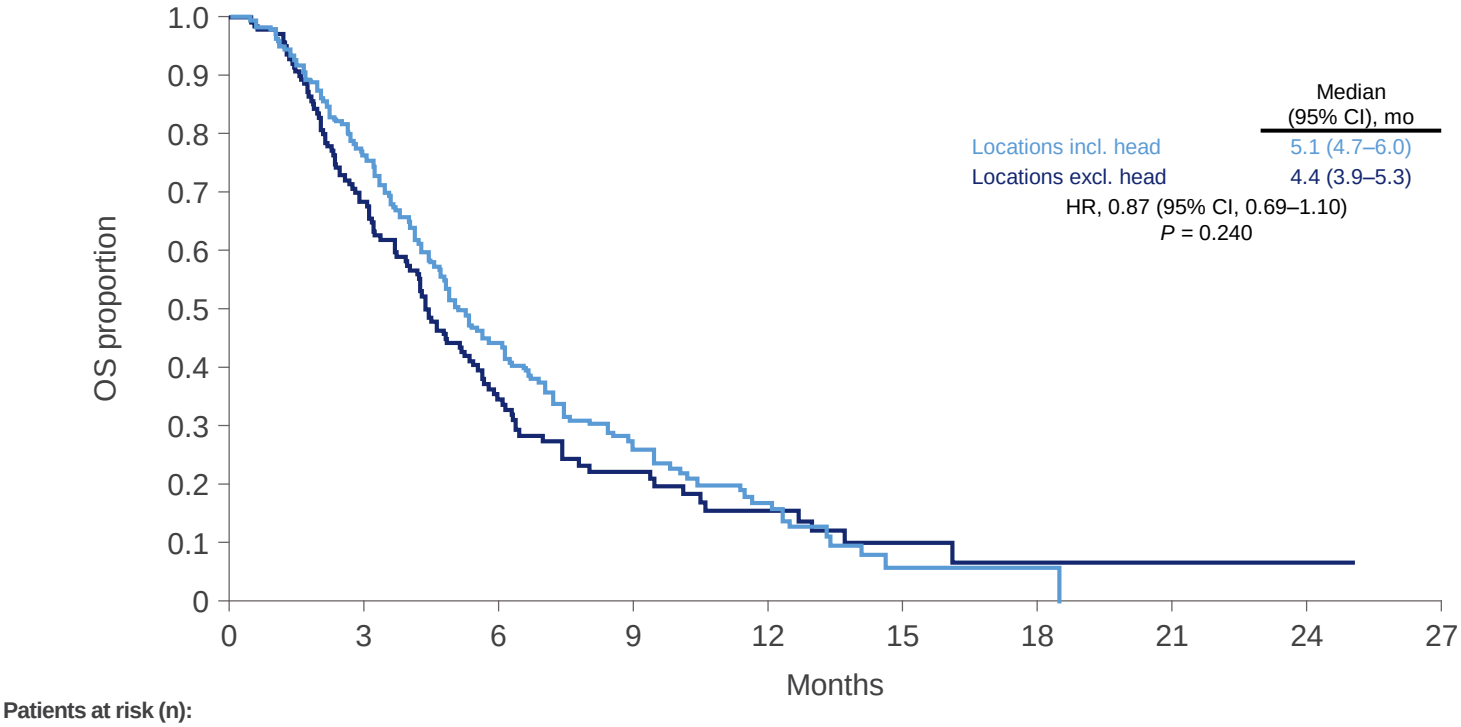
	Overall			
	1 (n = 81)	**2 (n = 184)**	**3 (n = 65)**	**>3 (n = 24)**
OS median, (95% CI), mo	6.1 (4.2–8.0)	4.6 (4.2–5.1)	4.8 (3.4–5.8)	2.7 (1.7–4.4)
HR* (95% CI)	–	1.59 (1.16–2.18)	1.38 (0.93– 2.03)	2.51 (1.49–4.21)
P†,‡		0.003	0.110	<0.001
PFS, median (95% CI), mo	2.9 (2.4–4.2)	1.6 (1.5–2.6)	2.3 (1.5–3.1)	1.4 (1.3–1.8)
HR* (95% CI)	–	1.56 (1.2–2.1)	1.22 (0.84–1.78)	2.04 (1.25–3.33)
P†,‡	–	0.003	0.302	0.004
ORR, %	9	8	5	8
	nal-IRI+5-FU/LV			
	1 (n = 19)	**2 (n = 49)**	**3 (n = 22)**	**>3 (n = 7)**
OS median, (95% CI), mo	6.1 (3.6–NR)	6.0 (4.6–8.5)	4.7 (3.2–7.1)	4.4 (1.0–NR)
HR* (95% CI)	–	1.31 (0.66–2.59)	1.42 (0.65–3.09)	1.36 (0.43–4.30)
P†,‡	–	0.441	0.380	P = 0.598
PFS, median (95% CI), mo	4.2 (1.4–7.0)	2.8 (1.4–4.0)	3.1 (1.4–5.6)	2.0 (1.1–9.3)
HR* (95% CI)	–	1.30 (0.70–2.41)	1.13 (0.55–2.34)	1.31 (0.47–3.67)
P †,‡		0.403	0.735	0.605
ORR, %	21	16	14	29

*Reference group for comparisons is '1 metastatic lesion'

†Cox model analysis with multiple groups

‡Two-sided *P* values from pairwise Fisher's exact test.

CI indicates confidence intervals; CR, complete response; HR, hazard ratio, NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.



Patients at risk (n):

Locations incl. head	256	189	98	36	17	2	1	0	0
Locations excl. head	146	95	40	19	10	3	2	1	1

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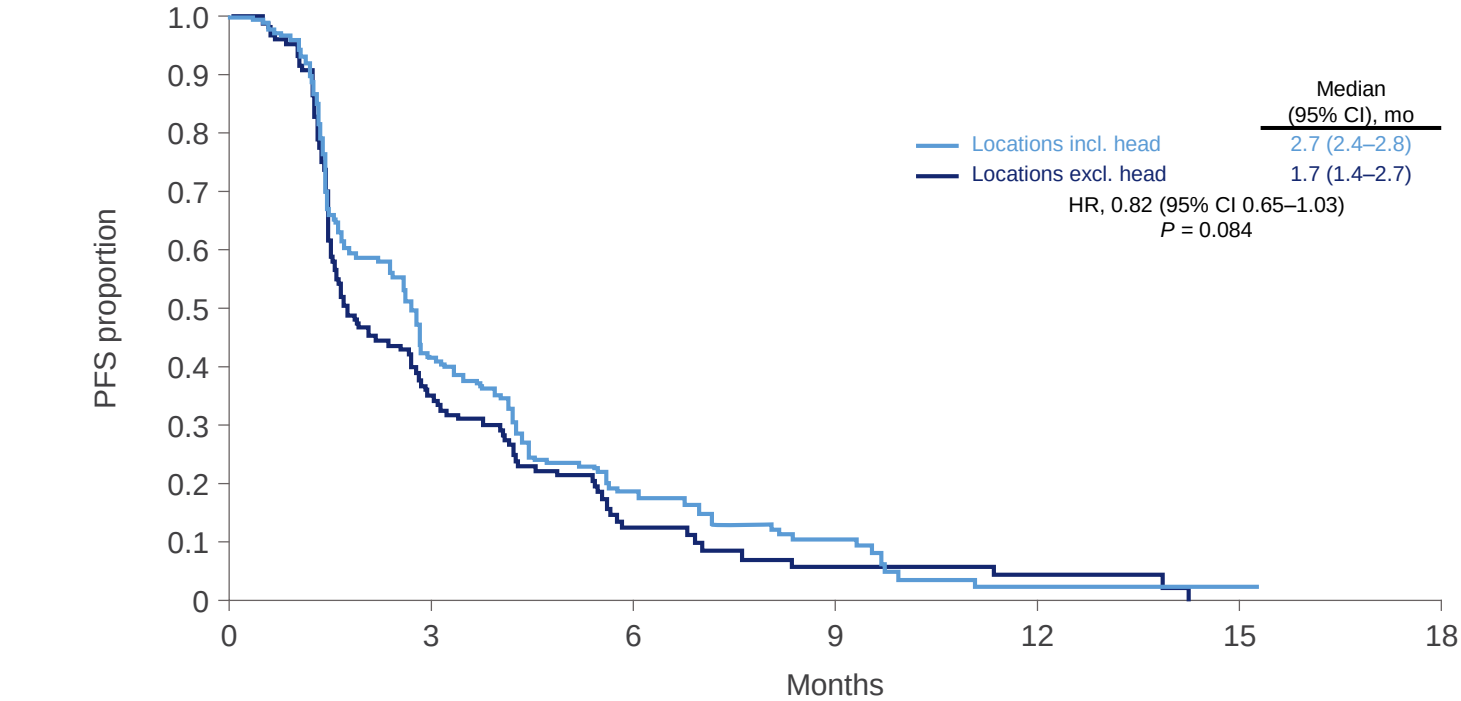


Patients at risk (n):

Locations incl. head	256	88	33	10	2	1
Locations excl. head	146	40	11	4	3	0

B

SUPPLEMENTAL FIGURE 1. Survival outcomes in patients with primary tumor locations including the pancreatic head versus excluding the head. A, Overall survival and B, Progression-free survival in patients with primary tumor locations including (incl.) the pancreatic head versus excluding (excl.) the head. CI, confidence interval; excl, excluding; HR, hazard ratio; incl., including; mo, months; mOS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 3. Effect of Disease Stage on Overall Survival in the NAPOLI-1 ITT Population and nal-IRI+5-FU/LV and 5-FU/LV Arms

	Stage III			Stage IV		
Disease Stage at Diagnosis	**All ITT (n = 75)**	**nal-IRI+ 5-FU/LV (n = 21)**	**5-FU/LV (n = 19)**	**All ITT (n = 213)**	**nal-IRI+ 5-FU/LV (n = 61)**	**5-FU/LV (n = 62)**
OS, median (95% CI), mo	6.3 (5.0–4.3)	9.0 (4.2–NR)	7.0 (3.4–9.4)	4.2 (3.7–4.7)	4.7 (4.2–5.6)	3.1 (2.2–4.2)
HR* (95% CI)	0.57 (0.42–0.78)	0.43 (0.21–0.88)	0.49 (0.25–0.96)	–	–	–
P	<0.001	0.021	0.039	–	–	–
ORR, %	9	14	5	6	16	0

*Versus Stage IV.

CI indicates confidence interval; HR, hazard ratio; ITT, intent-to-treat; NR, not reached; ORR, objective response rate; OS, overall survival.

SUPPLEMENTAL TABLE 4. Effect of Prior Surgery on Overall Survival in the NAPOLI-1 ITT Population

	Prior Surgery	
	Yes (n = 142)	**No (n = 275)**
OS, median (95% CI), mo	6.8 (5.8–7.5)	4.4 (4.1–4.8)
HR (95% CI)	0.62 (0.49–0.79)	
*P**	<0.001	
PFS, median (95% CI), mo	2.7 (2.0–3.4)	2.2 (1.6–2.8)
HR (95% CI)	0.84 (0.66–3.42)	
*P**	0.129	
ORR, %	6	8
P†	0.545	
CA 19-9 response, n/N (%)‡	26/111 (23)	43/214 (20)
P†	0.479	

*Log-rank *P* value

†*P* value from pairwise Fisher's exact test

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement.

CI indicates confidence interval; HR, hazard ratio; ITT, intent-to-treat; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 5. Effect of Prior Whipple Procedure on Efficacy Outcomes in the NAPOLI-1 ITT Population

	Prior Whipple	
	Yes (n = 113)	**No (n = 304)**
OS, median (95% CI), mo	6.1 (4.9–7.2)	4.6 (4.2–5.1)
HR (95% CI)	0.74 (0.57–0.95)	
*P**	0.020	
PFS, median (95% CI), mo	2.6 (1.9–3.1)	2.3(1.6–2.8)
HR (95% CI)	0.96 (0.75–1.22)	
*P**	0.725	
ORR, %	6	7
P†	0.830	
CA 19-9 response, n/N (%)‡	14/86 (16)	55/239 (23)
P†	0.220	

*Log-rank *P* value

†*P* value from pairwise Fisher's exact test

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement

CI indicates confidence interval; HR, hazard ratio; ITT, intent-to-treat; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 6. Survival Outcomes in Patient Subgroups Defined by Presence of a Biliary Stent in the ITT Population and NAPOLI-1 Treatment Arm

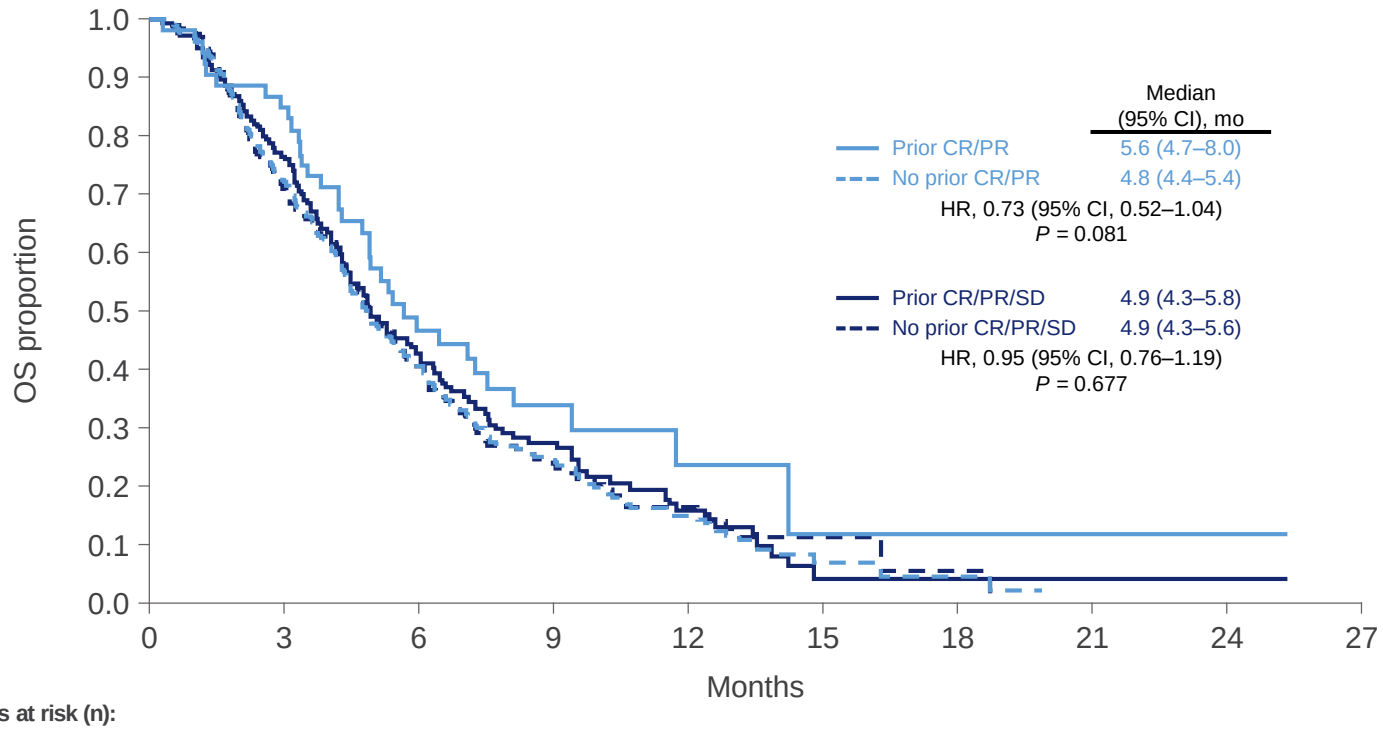
	Comparison by Baseline Stent (With Versus Without)			
	All Patients		nal-IRI+5-FU/LV	
	Baseline Stent With n = 37	Baseline Stent Without n = 380	Baseline Stent With n = 15	Baseline Stent Without n = 102
OS, median (95% CI), mo	5.3 (4.1–7.4)	4.8 (4.4–5.4)	6.2 (4.7–10.2)	6.1 (4.6–8.5)
HR (95% CI)	0.97 (0.65–1.46)		0.91 (0.47–1.78)	
*P**	0.895		0.785	
PFS, median (95% CI), mo	3.5 (1.6–4.4)	2.4 (1.7–2.7)	4.5 (2.8–6.8)	3.0 (2.0–4.1)
HR (95% CI)	0.82 (0.56–1.20)		0.79 (0.43–1.47)	
*P**	0.319		0.471	
ORR, %	16	6	27	15
P†	0.033		0.263	
CA 19-9 response, n/N (%)‡	10/27 (37)	59/298 (20)	5/12 (42)	22/83 (27)
P†	0.048		0.312	

*Log-rank *P* value

†*P* value from pairwise Fisher's exact test

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement

CI indicates confidence interval; HR, hazard ratio; ITT, intent to treat; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.



Patients at risk (n):

Prior CR/PR	55	44	20	9	4	1	1	1	1
No prior CR/PR	362	251	125	48	23	4	2	0	0
Prior CR/PR/SD	211	155	74	29	13	2	2	1	1
No prior CR/PR/SD	206	140	71	28	14	3	1	0	0

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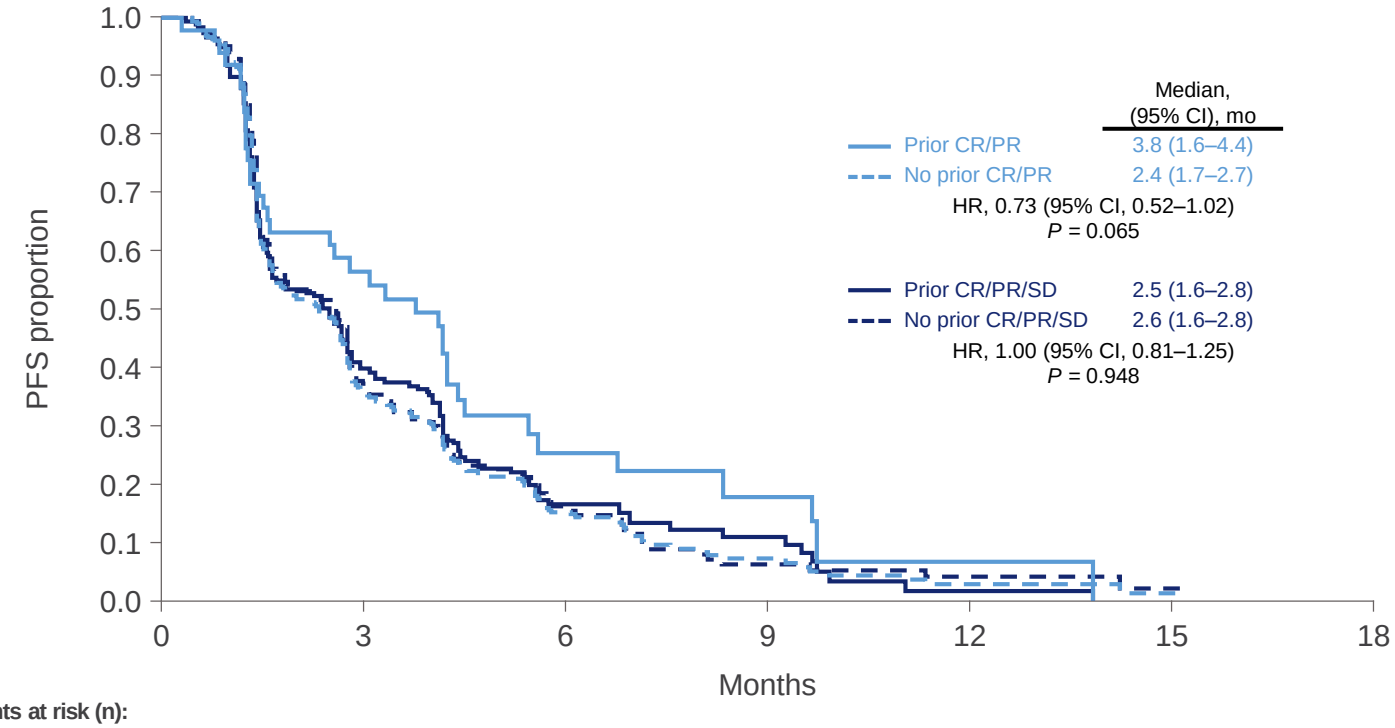
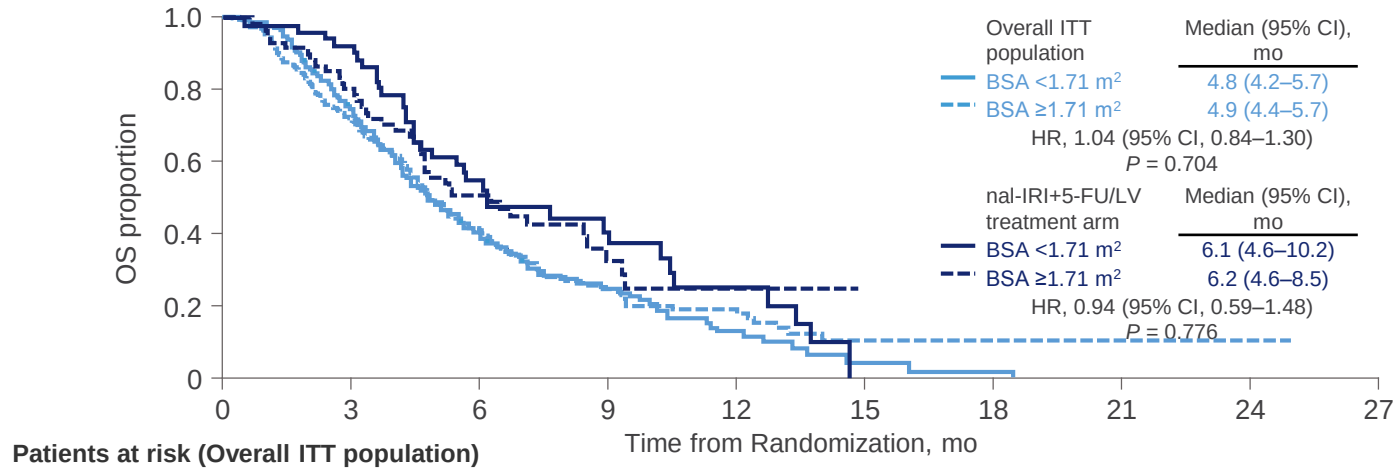


Patients at risk (n):

Prior CR/PR	55	24	8	4	1	0
No prior CR/PR	362	107	37	10	4	1
Prior CR/PR/SD	211	69	23	8	1	0
No prior CR/PR/SD	206	62	22	6	4	1

B

SUPPLEMENTAL FIGURE 2. Effect of best response to prior anticancer therapy on survival outcomes in the NAPOLI-1 ITT population. A. Overall survival and B. Progression-free survival in prior therapy response subgroups. CI, confidence interval; CR, complete response; HR, hazard ratio; ITT, intent-to-treat; mo, months; mOS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease.



Patients at risk (Overall ITT population)

BSA <1.71 m²	202	146	64	27	11	2	1	0	0
BSA ≥1.71 m²	215	149	81	30	16	3	2	1	1

Patients at risk (nal-IRI+5-FU/LV arm)

BSA <1.71 m²	55	48	22	11	5
BSA ≥1.71 m²	62	49	29	9	3

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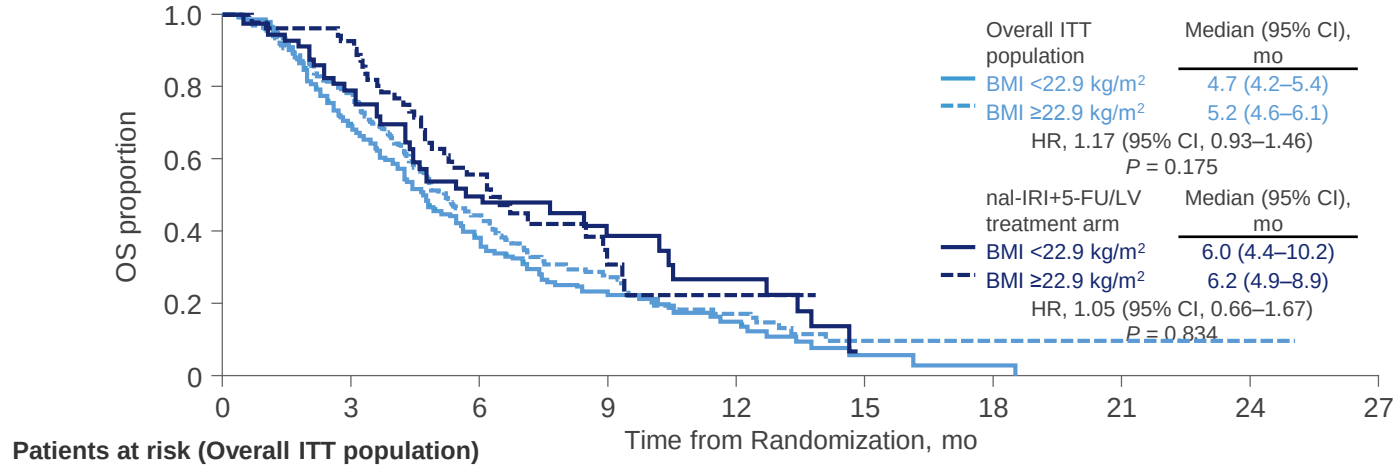


Patients at risk (Overall ITT population)

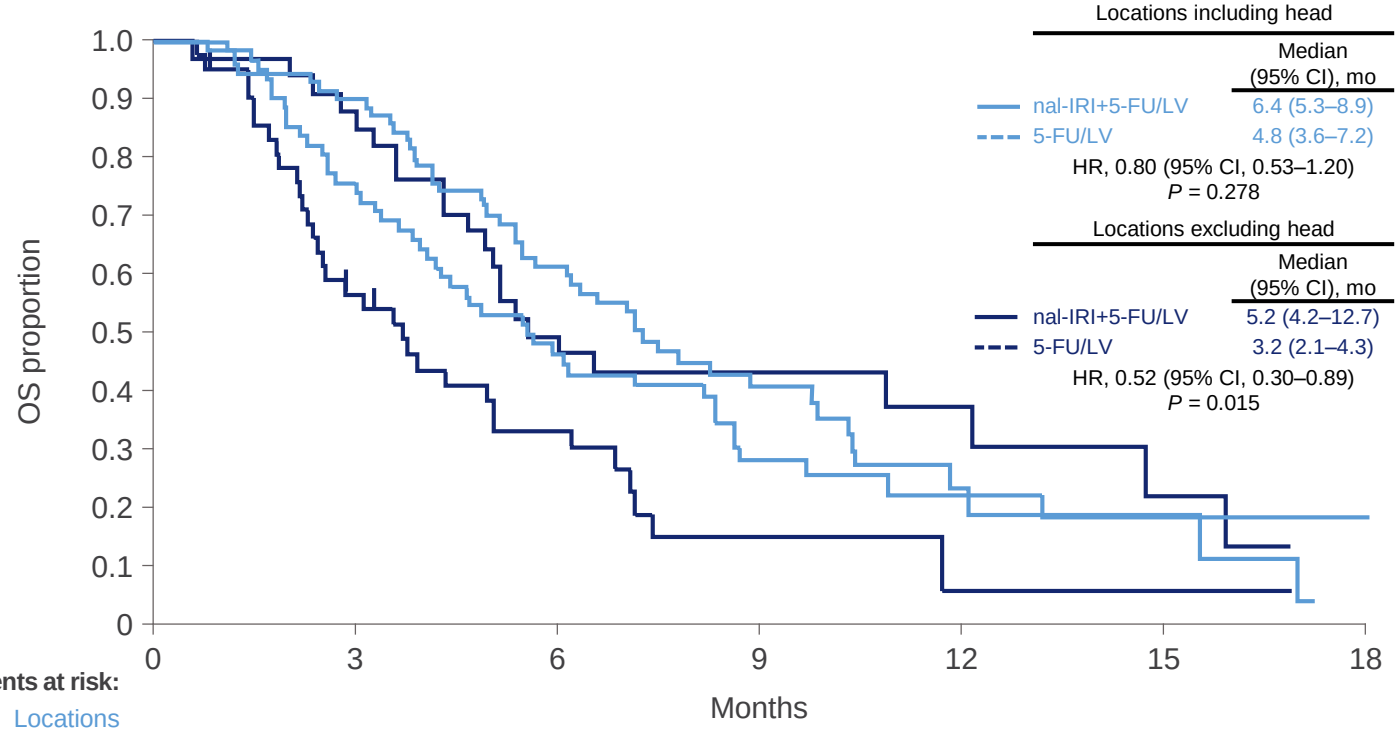
BMI <22.9 kg/m²	208	136	60	22	12	2	1
BMI ≥22.9 kg/m²	209	159	85	35	15	3	2

Patients at risk (nal-IRI+5-FU/LV arm)

BMI <22.9 kg/m²	59	44	22	12	6
BMI ≥22.9 kg/m²	58	53	29	8	2

B

SUPPLEMENTAL FIGURE 3. Overall survival in the NAPOLI-1 ITT population and nal-IRI+5-FU/LV arm by baseline weight parameters. Overall survival in patients subgroups divided by (A) BSA, and (B) BMI. ITT population includes all treatment arms. BMI, body mass index; BSA, body surface area; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; mo, months; mOS, overall survival.



Patients at risk:

Locations including head						
nal-IRI+5-FU/LV	76	63	36	11	4	0
5-FU/LV	69	45	26	9	5	1
Locations excluding head						
nal-IRI+5-FU/LV	35	29	12	8	4	0
5-FU/LV	48	22	8	2	1	0

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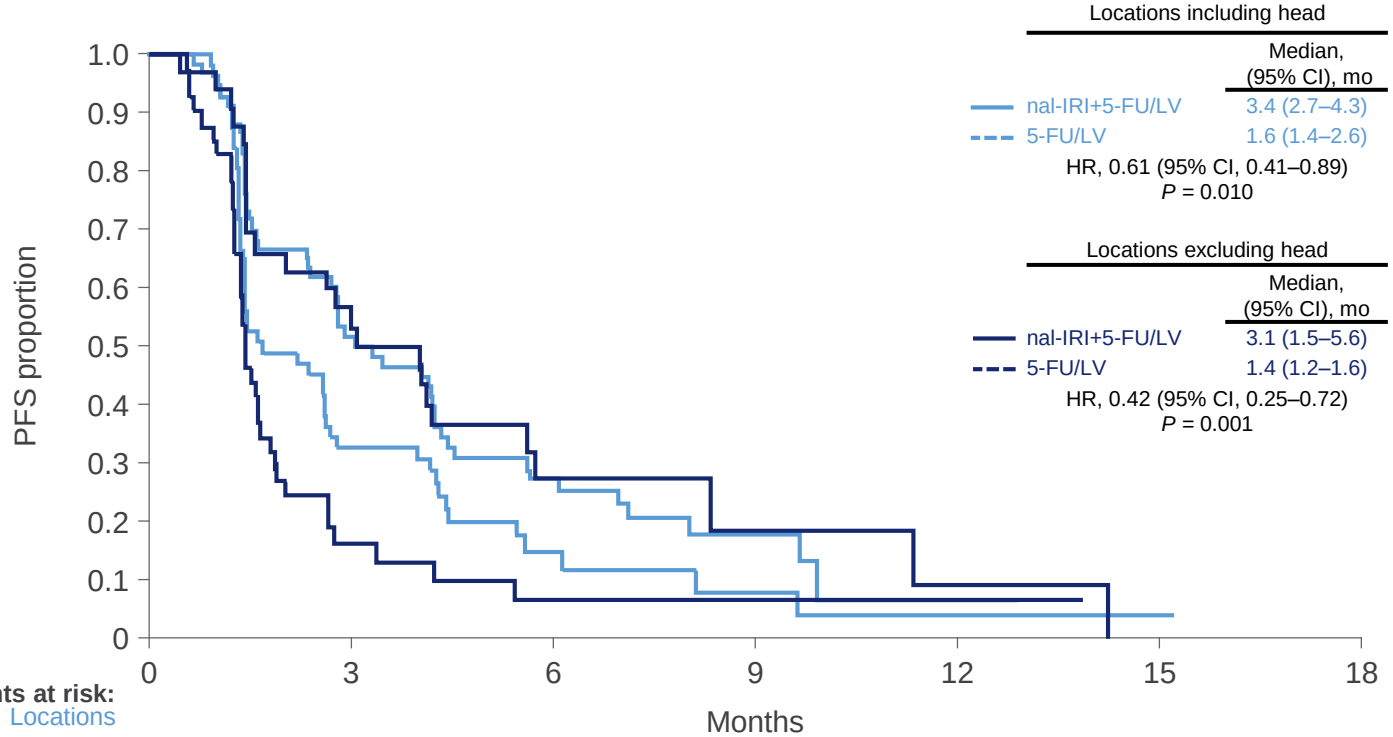
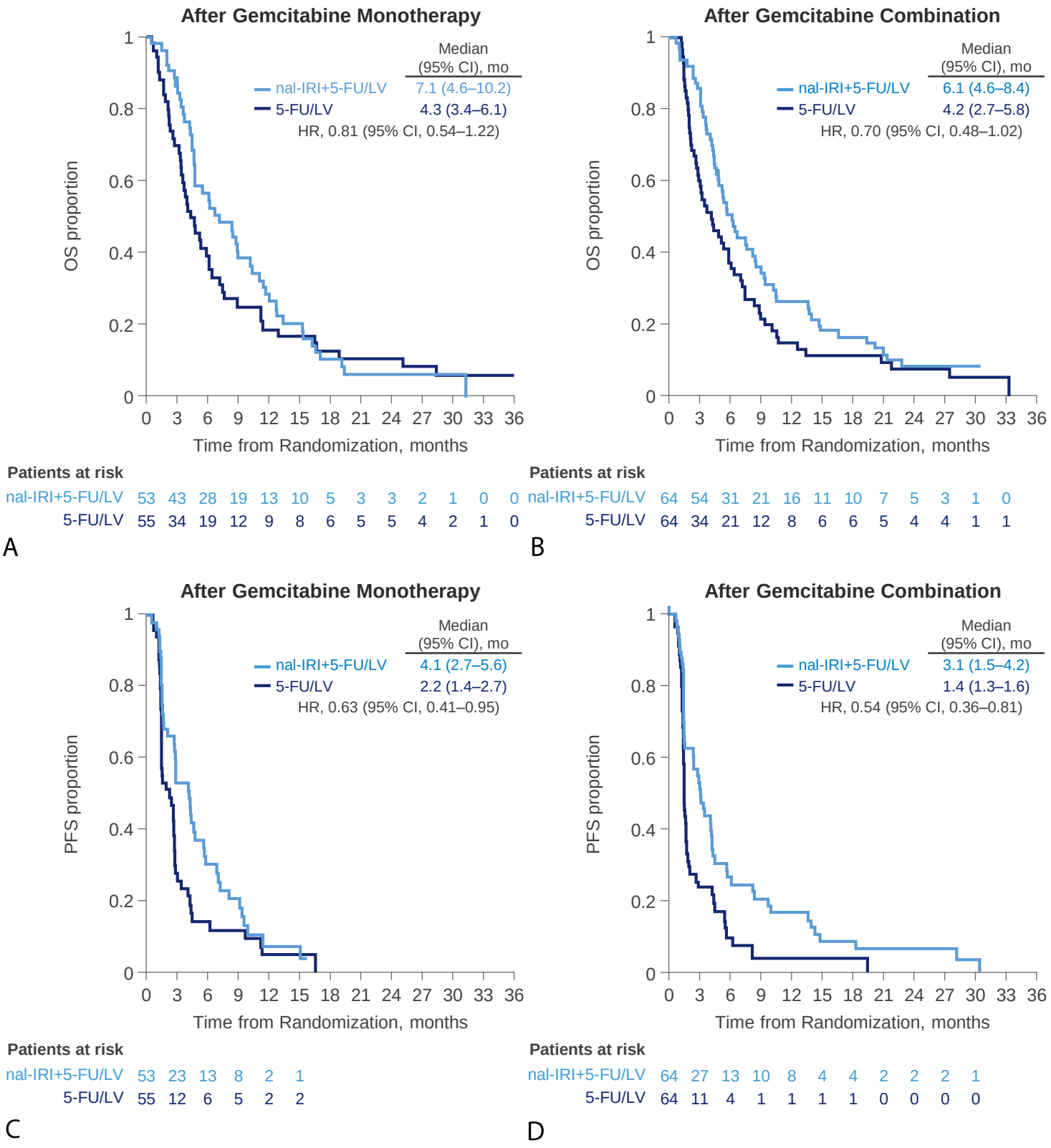


Patients at risk:

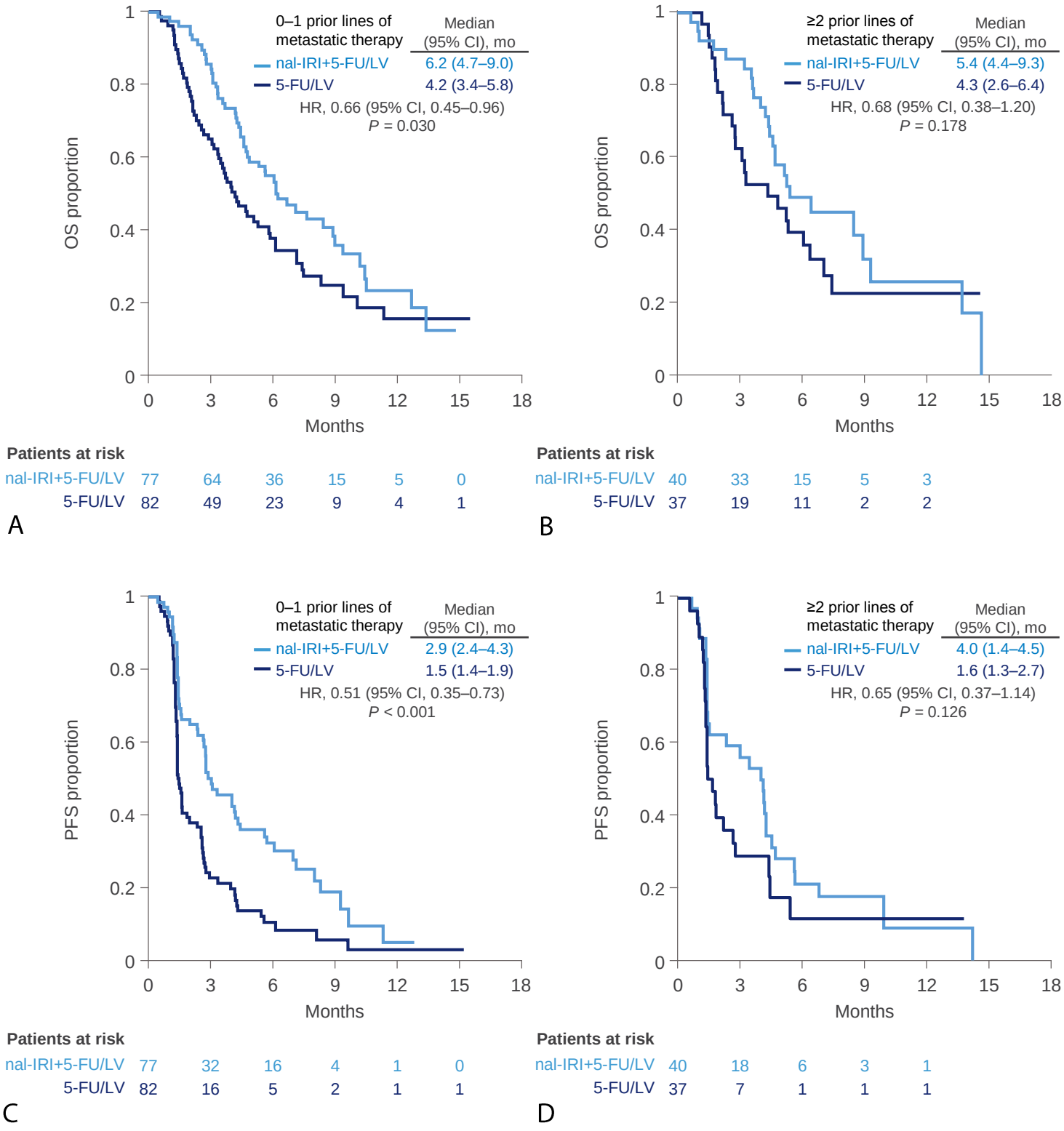
Locations including head						
nal-IRI+5-FU/LV	76	33	17	5	1	0
5-FU/LV	69	18	5	2	1	1
Locations excluding head						
nal-IRI+5-FU/LV	35	16	5	2	1	0
5-FU/LV	48	5	1	1	1	0

B

SUPPLEMENTAL FIGURE 4. Effect of nal-IRI+5-FU/LV versus 5-FU/LV on survival outcomes in patients with primary tumor locations including the pancreatic head versus excluding the head. A, Overall survival and (B) progression-free survival in patients with primary tumour locations including the pancreatic head versus excluding the head. CI, confidence interval; HR, hazard ratio; mo, months; OS, overall survival; PFS, progression-free survival.



SUPPLEMENTAL FIGURE 5. Survival outcomes in patients who had received prior gemcitabine monotherapy or combination therapy with nal-IRI+5-FU/LV versus 5-FU/LV. A, OS in patients with prior gemcitabine monotherapy treatment. B, OS in patients with prior gemcitabine combination treatment. C, PFS in patients with prior gemcitabine monotherapy. D, PFS in patients with prior gemcitabine combination therapy. CI, confidence interval; HR, hazard ratio; mo, month, OS, overall survival; PFS, progression-free survival.



SUPPLEMENTAL FIGURE 6. Survival outcomes in patients with 0–1 or ≥2 prior lines of metastatic therapy treated with nal-IRI+5-FU/LV versus 5-FU/LV. A, Overall survival in patients with 0–1 prior metastatic therapy lines. B, Overall survival in patients with ≥2 prior metastatic therapy lines. C, Progression-free survival in patients with 0–1 prior metastatic therapy lines. D, Progression-free survival in patients with ≥2 prior metastatic therapy lines. CI, confidence interval; HR, hazard ratio; mo, month, OS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 7. Efficacy of nal-IRI+5-FU/LV Versus 5-FU/LV Alone in Patients With 0–1 or ≥2 Prior Lines of Metastatic Treatment

	0–1 Prior Lines of Metastatic Therapy		≥2 Prior Lines of Metastatic Therapy	
	nal-IRI+5-FU/LV (n = 77 [66%])	**5-FU/LV (n = 82 [69%])**	**nal-IRI+5-FU/LV (n = 40 [34%])**	**5-FU/LV (n = 37 [31%])**
OS, median (95% CI), mo	6.2 (4.7–9.0)	4.2 (3.4–5.8)	5.4 (4.4–9.3)	4.3 (2.6–6.4)
HR (95% CI)	0.66 (0.45–0.96)		0.68 (0.38–1.20)	
*P**	0.030		0.180	
PFS, median, (95% CI), mo	2.9 (2.4–4.3)	1.5 (1.4–1.9)	4.0 (1.4–4.5)	1.6 (1.4–2.7)
HR (95% CI)	0.51 (0.35–0.73)		0.65 (0.4–1.1)	
*P**	<.001		0.126	
ORR, %	18	1	13	0
P†	<0.001		0.055	
CA 19-9, n/N (%)‡	21/68 (31)	6/56 (11)	7/29 (24)	1/25 (4)
P†	0.008		0.056	

*Log-rank *P* value.

†*P* value from pairwise Fisher's exact test.

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement.

CI indicates confidence interval; HR, hazard interval; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 8. Effect of Treatment With nal-IRI+5-FU/LV Versus 5-FU/LV in Patients With or Without Prior Surgery

	Prior Surgery			
	Yes		No	
	nal-IRI+5-FU/LV (n = 40)	5-FU/LV (n = 43)	nal-IRI+5-FU/LV (n = 77)	5-FU/LV (n = 76)
OS, median (95% CI), mo	8.4 (6.0–10.4)	6.1 (3.8–9.4)	5.3 (4.4–6.7)	3.4 (2.6–4.8)
HR (95% CI)	0.84 (0.48–1.48)		0.56 (0.38–0.82)	
P	0.547		0.003	
PFS, median (95% CI), mo	2.8 (1.4–7.0)	2.6 (1.4–4.0)	3.3 (2.8–4.2)	1.4 (1.3–1.5)
HR (95% CI)	0.72 (0.43–1.23)		0.47 (0.32–0.68)	
P	0.217		<0.001	
ORR, %	13	0	18	1
P†	0.023		<0.001	
CA 19-9 response, n/N (%)‡	10/32 (31)	4/31 (13)	17/63 (27)	4/51 (8)
P†	0.129		0.014	

*Log-rank *P* value.

†*P* value from pairwise Fisher's exact test.

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement.

CI indicates confidence interval; HR, hazard ratio; ITT, intent-to-treat; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 9. Effect of Treatment With nal-IRI+5-FU/LV Versus 5-FU/LV in Patients With or Without Prior Whipple Procedure

	Prior Whipple Procedure			
	Yes		No	
	nal-IRI+5-FU/LV (n = 30)	5-FU/LV (n = 33)	nal-IRI+5-FU/LV (n = 87)	5-FU/LV (n = 86)
OS, median (95% CI), mo	7.1 (4.6–10.2)	7.4 (4.0–NR)	5.7 (4.7–8.9)	3.4 (2.6–4.8)
HR (95% CI)	1.23 (0.65–2.33)		0.50 (0.35–0.73)	
*P**	0.533		<0.001	
PFS, median (95% CI), mo	2.3 (1.4–4.3)	2.6 (1.4–4.2)	4.0 (2.8–4.2)	1.4 (1.3–1.6)
HR (95% CI)	1.07 (0.60–1.90)		0.43 (0.30–0.61)	
*P**	0.836		<0.001	
ORR, %	10	0	18	1
P†	0.102		<0.001	
CA 19-9 response, n/N (%)‡	4/23 (17)	3/22 (14)	23/72 (32)	5/60 (8)
P†	1.000		0.001	

*Log-rank *P* value.

†*P* value from pairwise Fisher's exact test.

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement.

CI indicates confidence interval; HR, hazard ratio; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 10. Efficacy Outcomes in Patient Subgroups With or Without Biliary Stents at Baseline Treated With nal-IRI+5-FU/LV Versus 5-FU/LV

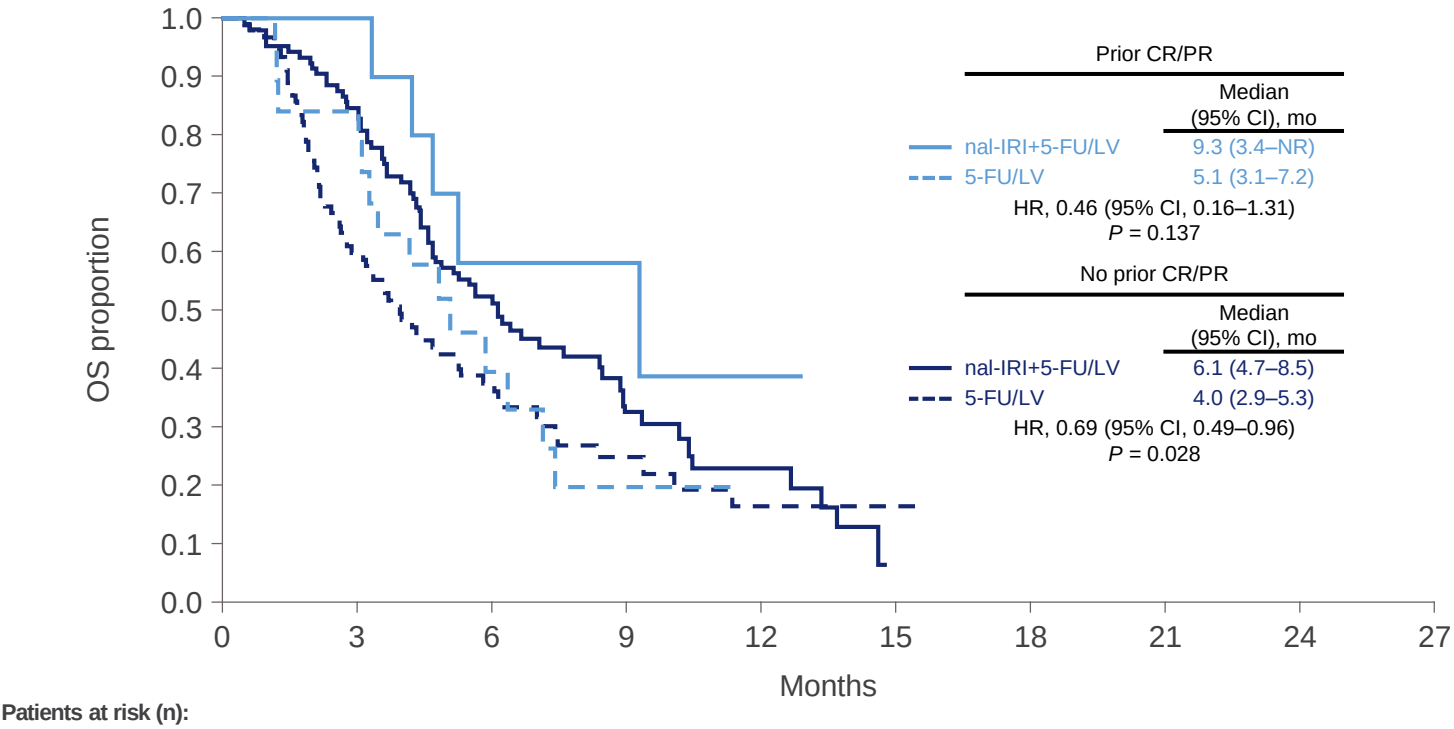
	Comparison by Treatment Group			
	Baseline Stent: With		Baseline Stent: Without	
	nal-IRI+5-FU/LV (n = 15)	5-FU/LV (n = 8)	nal-IRI+5-FU/LV (n = 102)	5-FU/LV (n = 111)
OS, median (95% CI), mo	6.2 (4.7–10.2)	5.2 (1.7–7.4)	6.1 (4.6–8.5)	4.2 (3.2–5.3)
HR (95% CI)	0.44 (0.14–1.43)		0.68 (0.49–0.95)	
*P**	0.156		0.022	
PFS, median (95% CI), mo	4.5 (2.8–6.8)	1.5 (1.2–NR)	3.0 (2.0–4.1)	1.5 (1.4–1.9)
HR (95% CI)	0.21 (0.06–0.75)		0.59 (0.43–0.81)	
*P**	0.009		<0.001	
ORR, %	27	0	15	1
P†	0.257		<0.001	
CA 19-9 response, n/N (%)‡	5/12 (42)	2/5 (40)	22/83 (27)	6/77 (8)
P†	1.000		0.002	

*Log-rank *P* value.

†*P* value from pairwise Fisher's exact test.

‡Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement.

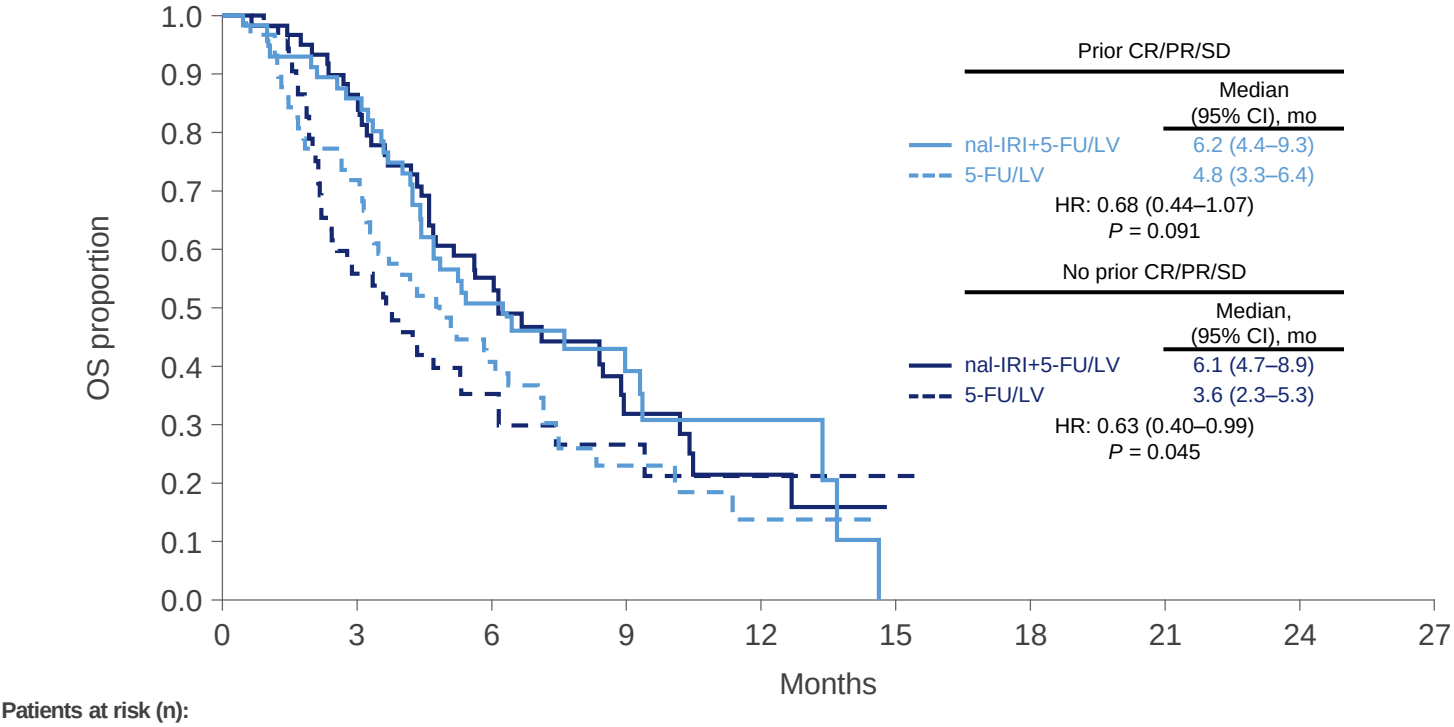
CI indicates confidence interval; HR, hazard ratio; mOS, overall survival; NR, not reached; ORR, objective response rate; PFS, progression-free survival.



Patients at risk (n):

nal-IRI+5-FU/LV	11	10	4	3	1	0
5-FU/LV	21	16	6	1	0	0
nal-IRI+5-FU/LV	106	87	47	17	7	0
5-FU/LV	98	52	28	10	6	1

A



Patients at risk (n):

nal-IRI+5-FU/LV	58	47	23	10	4	0
5-FU/LV	61	40	21	5	2	0
nal-IRI+5-FU/LV	59	50	28	10	4	0
5-FU/LV	58	28	13	6	4	1

B

SUPPLEMENTAL FIGURE 7. Effect of treatment with nal-IRI+5-FU/LV versus 5-FU/LV on overall survival in patients with or without prior CR/PR or CR/PR/SD. A, Overall survival in patients with or without prior CR/PR as best response. B, Overall survival in patients with or without prior CR/PR/SD as best response. CI, confidence interval; CR, complete response; HR, hazard ratio; mo, months; NR, not reached; OS, overall survival PR, partial response; SD, stable disease.

SUPPLEMENTAL TABLE 11. Efficacy of nal-IRI+5-FU/LV Versus 5-FU/LV Treatment Within Metabolism and Nutrition Disorder Subgroups at Baseline

	nal-IRI+5-FU/LV / 5-FU/LV									
	Metabolism and Nutrition Disorders		**Diabetes Mellitus and/or Type 2 Diabetes Mellitus**		**Decreased Appetite***		**Hypercholesterolemia**		**Hypercholesterolemia and/or Hyperlipidemia and/or Dyslipidemia**	
	With n = 71/77	**Without n = 46/42**	**With n = 42/49**	**Without n = 75/70**	**With n = 21/23**	**Without n = 96/96**	**With n = 13/9**	**Without n = 104/110**	**With n = 22/21**	**Without n = 95/98**
mOS										
HR (95% CI)	0.53 (0.36–0.78)	1.05 (0.61–1.82)	0.69 (0.42–1.12)	0.67 (0.44–1.01)	0.46 (0.23–0.95)	0.74 (0.52–1.05)	0.51 (0.20–1.32)	0.67 (0.48–0.94)	0.58 (0.29–1.15)	0.67 (0.47–0.96)
P†	0.001	0.853	0.133	0.052	0.032	0.089	0.151	0.019	0.112	0.029
PFS										
HR (95% CI)	0.47 (0.32–0.68)	0.69 (0.41–1.15)	0.53 (0.33–0.87)	0.57 (0.39–0.83)	0.24 (0.11–0.54)	0.59 (0.42–0.83)	0.43 (0.16–1.19)	0.56 (0.40–0.77)	0.34 (0.16–0.72)	0.59 (0.42–0.82)
P†	<0.001	0.157	0.011	0.003	<0.001	0.002	0.090	<0.001	0.003	0.002
ORR, %	20/0	11/2	21/0	13/1	29/0	14/1	15/0	16/1	14/0	17/1
P‡	<0.001	0.205	<0.001	0.009	0.008	0.001	0.494	<0.001	0.233	<0.001
CA 19-9 response, %§	31/7	25/15	22/9	33/11	37/0	26/13	18/0	30/11	24/6	29/11
CA 19-9 evaluable patients	59/56	36/26	37/35	58/47	19/18	76/64	11/6	84/76	17/16	78/66
P‡	0.002	0.529	0.191	0.010	0.008	0.056	0.515	0.003	0.335	0.007

*Includes anorexia, poor appetite, lack of appetite and loss of appetite.

†Log-rank *P* value.

‡*P* value from pairwise Fisher's exact test.

§Response defined as ≥50% reduction in baseline CA 19-9 levels, in patients with baseline levels >30 U/ml and at least one post-baseline CA 19-9 measurement.

CI indicates confidence intervals. HR, hazard ratio; ORR, objective response rate; mOS, median overall survival; PFS, progression-free survival.

SUPPLEMENTAL TABLE 12. Safety Data in the NAPOLI-1 Safety Population*

	nal-IRI+5-FU/LV (n = 117)	5-FU/LV (n = 134)
Overall patients with TEAE grade ≥3	90 (76.9)	75 (56.0)
Patients with grade ≥3 nonhematologic TEAEs (present in >5% patients), %†		
Fatigue	14	4
Diarrhea	13	5
Vomiting	11	3
Nausea	8	3
Asthenia	8	7
Abdominal pain	7	6
Patients with grade ≥3 hematologic TEAEs based on laboratory values, %†‡		
Neutrophil count decreased	20	2
Hemoglobin decreased	6	5
Platelet count decreased	2	0
Patients with related TEAE leading to death		
All causes, %	2	7
Treatment-related, %	1	0
Number of patients with TEAEs resulting in, n (%)		
Dose reduction	33	4
Dose delays	62	32
Treatment discontinuation	11	8
Average relative dose intensity, %		
nal-IRI	83.2	–
5-FU	83.9	95.6
Average exposure, weeks§	15	10

*Patients receiving at least one dose of study drug.
†Common Terminology Criteria for Adverse Events Version 4.
‡Includes only patients who had at least one post-baseline assessment.
§Duration of exposure = (the time from the date of the last administration of study drug + projected days to next dose of study drug administration - date of first study drug administration)/7.
ITT indicates intent-to-treat; TEAE, treatment-emergent adverse event.