

Nanoliposomal irinotecan plus fluorouracil and folinic acid in irinotecan-pretreated vs. -naive pancreatic cancer patients: A retrospective cohort study

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Introduction

In the phase 3 NAPOLI-1 study⁵ from 2016, the liposomal encapsulated irinotecan (nanoliposomal irinotecan, nal-IRI) plus fluorouracil and folinic acid (5-FU/LV) significantly extended overall survival (6.1 vs. 4.2 months) in comparison to 5-FU/LV monotherapy in the treatment of metastatic pancreatic adenocarcinoma cancer (PAC) patients. In this study, only gemcitabine-pretreated patients were included. As the irinotecan-containing FOLFIRINOX regimen became a commonly applied first-line therapy in fit PAC patients, it remains unclear which benefit nal-IRI+5-FU/LV retains within this group.

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Method

This retrospective study of locally advanced or metastatic PAC patients who received nal-IRI+5-FU/LV between December 2016 and April 2021 is composed by two cohorts: An exploratory cohort of 16 patients treated in the University Medical Center Hamburg-Eppendorf (UKE) complemented by 69 patients from an oncologic practices chemotherapy registry ("Onkotrakt"). The merged cohort from both sources was analyzed regarding the impact of prior irinotecan therapy on median time to treatment failure (mTTF) of nal-IRI+5-FU/LV.

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Results

Table 1: Patient characteristics

UKE cohort/ total cohort (%)	16/85 (19)
Age – years (range)	67 (49 – 82)
Female sex – no. (%)	40/85 (47)
Median time to treatment failure – months	4.3

Table 2: Therapy characteristics

Applied cycles of nal-IRI+5-FU/LV - mean	9.5
≥2 Prior palliative regimens – no. (%)	40/85 (47)
Prior irinotecan-based palliative treatment – no. (%)	29/80 (36)
Prior surgery – no. (%)	21/81 (26)

Patients pretreated with an irinotecan-based palliative chemotherapy had a significant shorter mTTF compared to irinotecan-naive patients (3.2 vs. 4.6 months, $p = 0.04$). This effect decreased with distance from therapy onset to last applied irinotecan (mTTF ranges from 1.8 [<3 months] to 4.4 months [>12 months]). Notably, in an analysis of all patients, the effect of the number of prior palliative therapy lines before nal-IRI+5-FU/LV initiation was similar to irinotecan pretreatment (mTTF 3.2 [<2] vs. 4.9 months [≥ 2], $p = 0.007$).

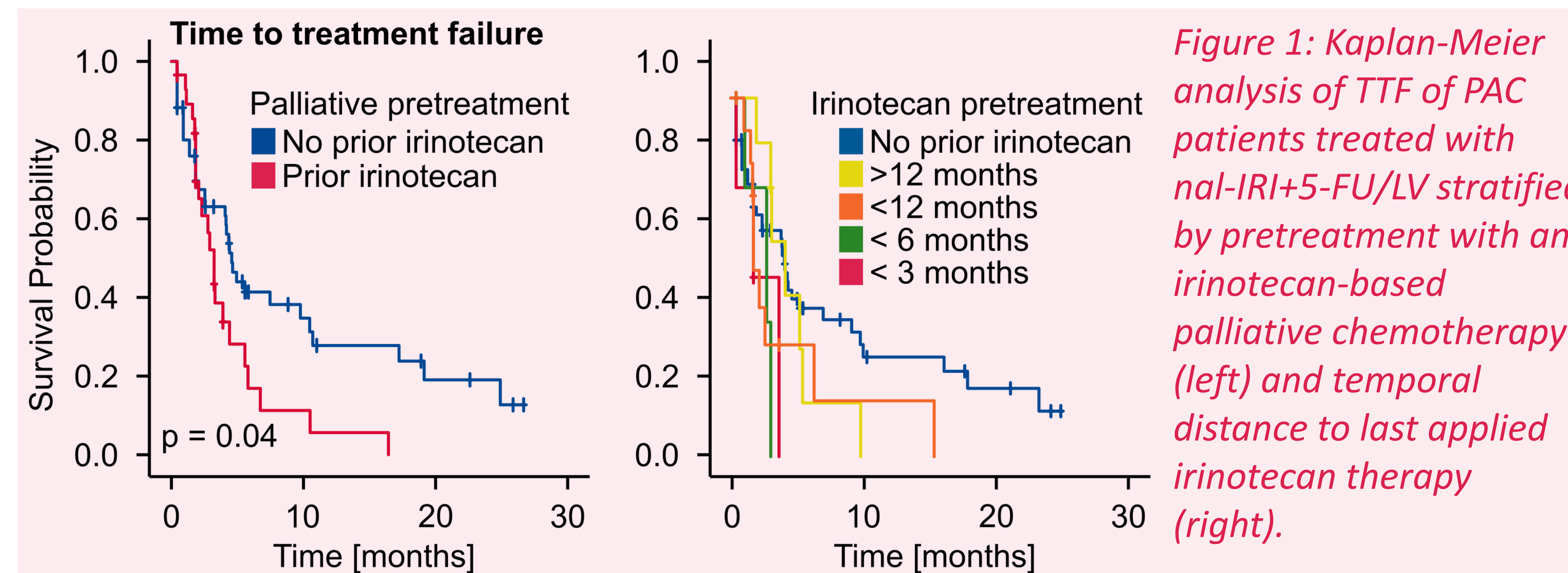


Table 3: Prognostic value of previous treatments in a uni- and multivariable analysis (cox proportional hazards model)*

	Univariable		Multivariable	
	HR (95% CI)	p	HR (95% CI)	p
≥2 Prior palliative regimens	2.0 (1.2-3.4)	0.009	1.3 (0.6-3.2)	0.5
Prior irinotecan-based palliative treatment	1.8 (1.0-3.1)	0.04	0.8 (0.4-1.8)	0.6
Prior 5-FU-based palliative treatment	2.3 (1.3-4.0)	0.003	2.2 (0.9-5.3)	0.09

* All available patient- and therapy characteristics were analyzed in an univariable analysis. Only significant factors are displayed and were further analyzed in a multivariable analysis

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Conclusion

This retrospective cohort analysis of nal-IRI+5-FU/LV-treated PAC patients is the first to directly compare this regimen in irinotecan-naive vs. -pretreated patients. Although mTTF was significantly shorter in irinotecan-pretreated patients, it still presents an important salvage treatment option in these patients. Expectedly treatment efficacy increases with time elapsed to last irinotecan exposure.

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References

5 Wang-Gillam et al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial. *Lancet*. 2016 Feb 6;387(10018):545-557

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