

**SUPPLEMENTARY MATERIAL**

**Supplementary Table 1. Resection rates and overall survival of selected studies on (m)FOLFIRINOX for localized pancreatic adenocarcinoma.**

Trial / First Author	Year	Country	Design	No. of patients receiving (m)FOLFIRINOX	Resection rate <sup>a</sup>	Median OS in months <sup>a</sup>
<b>PR PDAC</b>						
De Marsh <sup>1</sup>	2018	USA	Prospective cohort	21	81%	34
SWOG S1505 <sup>2</sup>	2021	USA	Randomized phase II trial	55	73%	23.2
TAPS cohort	2021	USA + The Netherlands	Retrospective	346	71%	31.2
<b>BR PDAC</b>						
Murphy <sup>3</sup>	2018	USA	Nonrandomized Phase II trial	48	67%	37.7
Janssen <sup>4</sup>	2019	USA, The Netherlands, France, UK, Scotland, Austria, Japan, Korea, Australia	Patient-level meta-analysis	283	68%	22.2
Maggino <sup>5</sup>	2019	Italy	Prospective cohort	107	34%	20.0
Yoo <sup>6</sup>	2020	South-Korea	Retrospective	75	36%	18.4
Garnier <sup>7</sup>	2020	France	Retrospective	199	45%	22 (BR and LA combined)
ESPAC-5F (abstract only) <sup>8</sup>	2020	UK	Randomized phase II trial	20	55%	NR 1 year OS 84%
Auclin <sup>9</sup>	2021	France	Retrospective	102	42%	26.8

ALLIANCE A021501 (abstract only) <sup>10</sup>	2021	USA	Randomized phase II trial	70 without RT 56 with RT	48% without RT 35% with RT	31.0 without RT 17.1 with RT
TAPS cohort LA PDAC	2021	USA + The Netherlands	Retrospective	531	53%	23.2
Suker <sup>11</sup>	2016	USA, France, UK, Austria	Patient-level meta-analysis	315	26%	24.2
Murphy <sup>12</sup>	2019	USA	Nonrandomized Phase II trial	49	69%	31.4
Maggino <sup>5</sup>	2019	Italy	Prospective cohort	153	12%	16.2
Yoo <sup>6</sup>	2020	South-Korea	Retrospective	124	29%	17.1
Garnier <sup>7</sup>	2020	France	Retrospective	59	14%	22 (BR and LA combined)
Walma <sup>13</sup>	2020	The Netherlands	Prospective	252	13%	14.0
Auclin <sup>9</sup>	2021	France	Retrospective	226	16%	18.9
JCOG1407 (abstract only) <sup>14</sup>	2021	Japan	Randomized phase II trial	62	NR	24.0
TAPS cohort	2021	USA + The Netherlands	Retrospective	958	18%	18.7

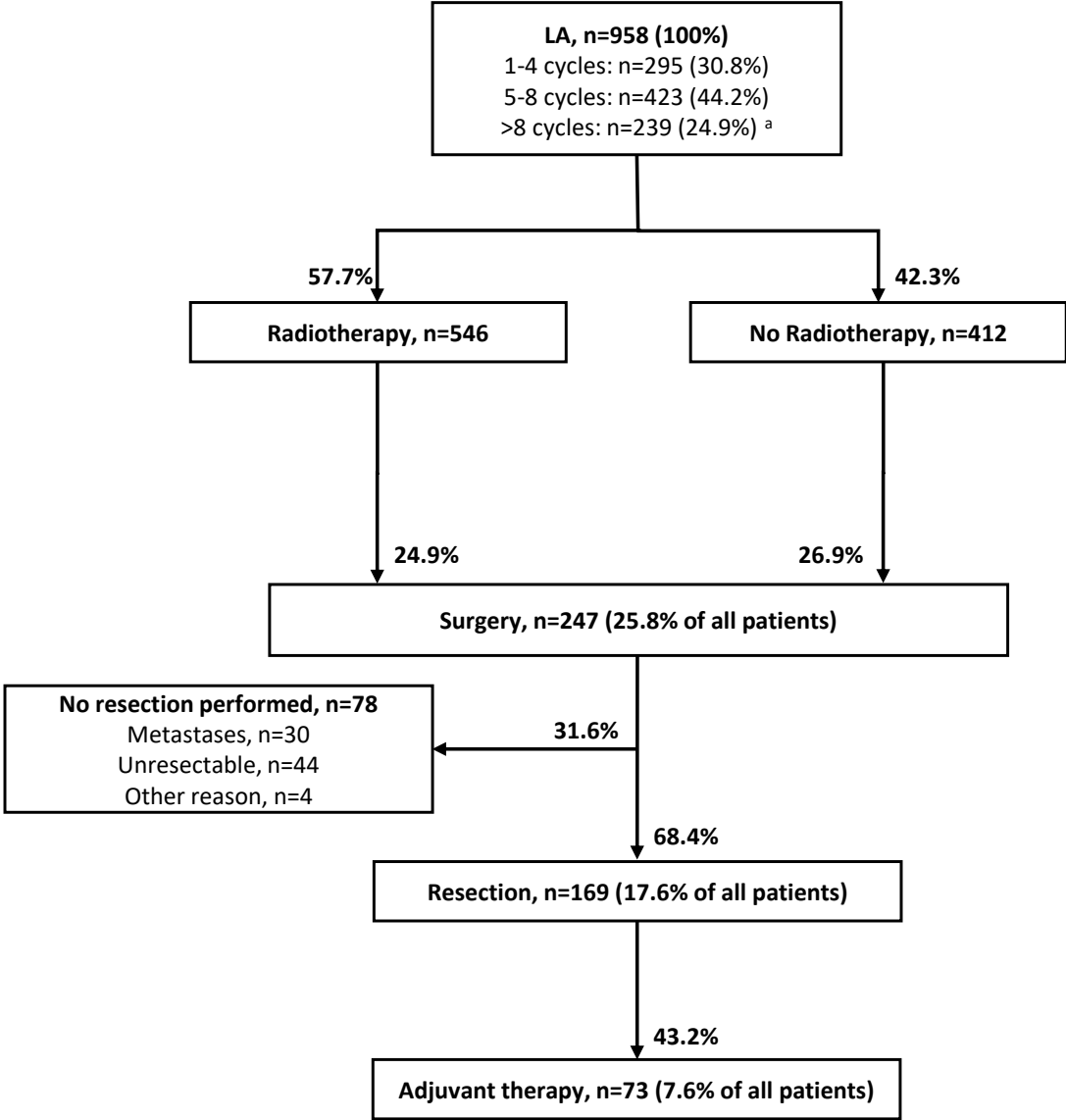
<sup>a</sup> Resection rate and survival for all enrolled patients in each study. BR = borderline resectable; LA = locally advanced; OS = overall survival; PDAC = pancreatic ductal adenocarcinoma; NR = not reported; PR = potentially resectable; RT = radiotherapy; UK = United Kingdom; US = United States of America

## References

1. de Marsh WR, Talamonti MS, Baker MS, *et al.* Primary systemic therapy in resectable pancreatic ductal adenocarcinoma using mFOLFIRINOX: A pilot study. *J Surg Oncol.* Mar 2018;117(3):354-362.
2. Sohal DPS, Duong M, Ahmad SA, *et al.* Efficacy of Perioperative Chemotherapy for Resectable Pancreatic Adenocarcinoma: A Phase 2 Randomized Clinical Trial. *JAMA Oncol.* Mar 1 2021;7(3):421-427.
3. Murphy JE, Wo JY, Ryan DP, *et al.* Total Neoadjuvant Therapy With FOLFIRINOX Followed by Individualized Chemoradiotherapy for Borderline Resectable Pancreatic Adenocarcinoma: A Phase 2 Clinical Trial. *JAMA Oncol.* Jul 1 2018;4(7):963-969.
4. Janssen QP, Buettner S, Suker M, *et al.* Neoadjuvant FOLFIRINOX in Patients With Borderline Resectable Pancreatic Cancer: A Systematic Review and Patient-Level Meta-Analysis. *JNCI: Journal of the National Cancer Institute.* 2019;111(8):782-794. doi:10.1093/jnci/djz073
5. Maggino L, Malleo G, Marchegiani G, *et al.* Outcomes of Primary Chemotherapy for Borderline Resectable and Locally Advanced Pancreatic Ductal Adenocarcinoma. *JAMA Surg.* Jul 24 2019;
6. Yoo C, Hwang I, Song TJ, *et al.* FOLFIRINOX in borderline resectable and locally advanced unresectable pancreatic adenocarcinoma. *Ther Adv Med Oncol.* 2020;12:1758835920953294.
7. Garnier J, Ewald J, Marchese U, *et al.* Borderline or locally advanced pancreatic adenocarcinoma: A single center experience on the FOLFIRINOX induction regimen. *Eur J Surg Oncol.* Aug 2020;46(8):1510-1515.
8. Ghaneh P, Palmer DH, Cicconi S, *et al.* ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer. *J Clin Oncol.* 2020;38(15\_suppl):4505-4505. doi:10.1200/JCO.2020.38.15\_suppl.4505
9. Auclin E, Marthey L, Abdallah R, *et al.* Role of FOLFIRINOX and chemoradiotherapy in locally advanced and borderline resectable pancreatic adenocarcinoma: update of the AGEO cohort. *Br J Cancer.* Mar 26 2021;
10. Katz MHG, Shi Q, Meyers JP, *et al.* Alliance A021501: Preoperative mFOLFIRINOX or mFOLFIRINOX plus hypofractionated radiation therapy (RT) for borderline resectable (BR) adenocarcinoma of the pancreas. *J Clin Oncol.* 2021;39(3\_suppl):377-377. doi:10.1200/JCO.2021.39.3\_suppl.377
11. Suker M, Beumer BR, Sadot E, *et al.* FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis. *Lancet Oncol.* Jun 2016;17(6):801-810.
12. Murphy JE, Wo JY, Ryan DP, *et al.* Total Neoadjuvant Therapy With FOLFIRINOX in Combination With Losartan Followed by Chemoradiotherapy for Locally Advanced Pancreatic Cancer: A Phase 2 Clinical Trial. *JAMA Oncol.* Jul 1 2019;5(7):1020-1027.
13. Walma MS, Brada LJ, Patuleia SIS, *et al.* Treatment strategies and clinical outcomes in consecutive patients with locally advanced pancreatic cancer: A multicenter prospective cohort. *Eur J Surg Oncol.* Nov 26 2020;
14. Ozaka M, Ueno M, Ishii H, *et al.* Randomized phase II study of modified FOLFIRINOX versus gemcitabine plus nab-paclitaxel combination therapy for locally advanced pancreatic cancer (JCOG1407). *J Clin Oncol.* 2021;39(15\_suppl):4017-4017. doi:10.1200/JCO.2021.39.15\_suppl.4017

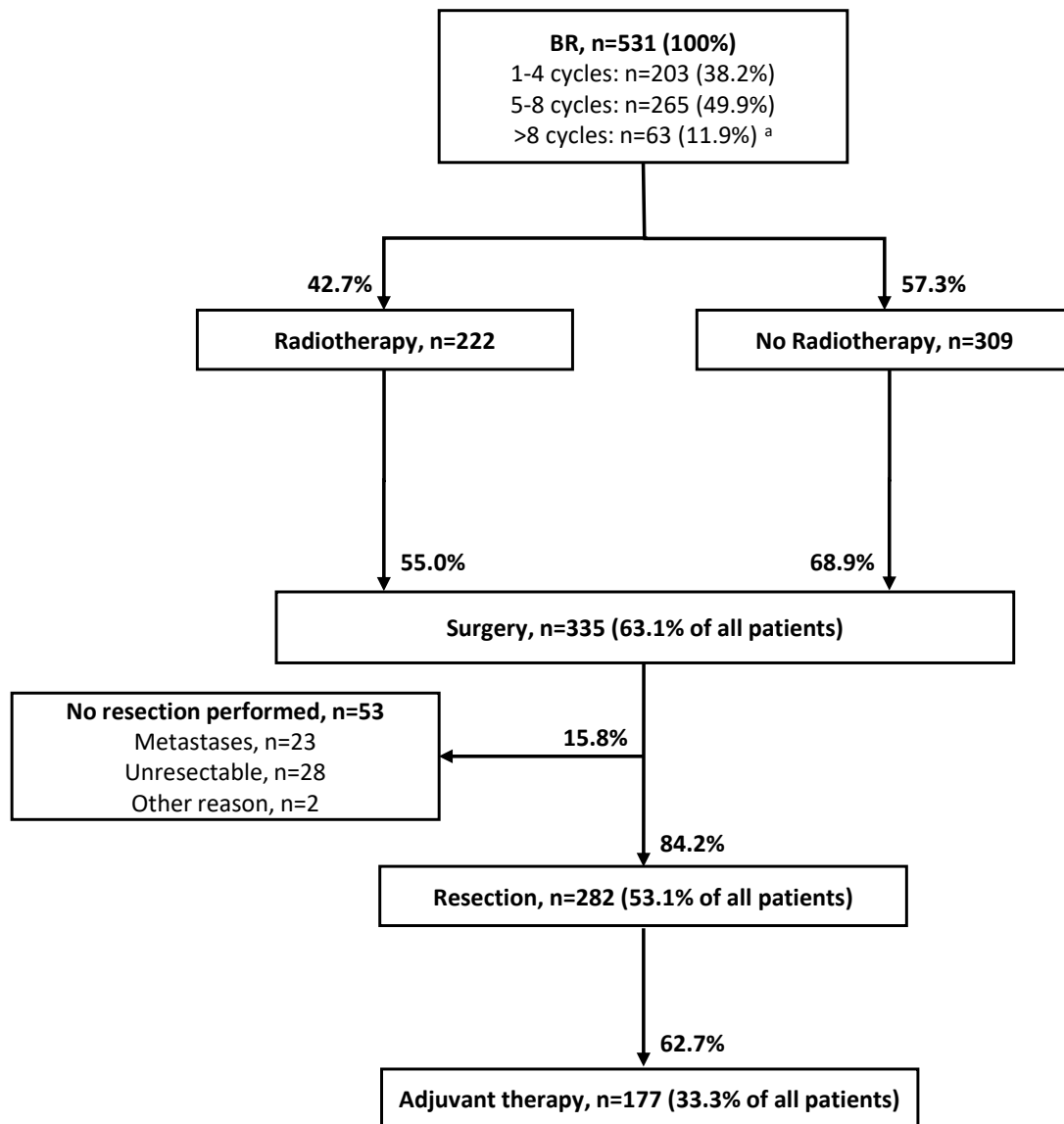
**Supplementary Figure 1. Flow chart and alluvial diagram of treatment for patients with localized pancreatic adenocarcinoma who started treatment with (m)FOLFIRINOX by stage.**

A)



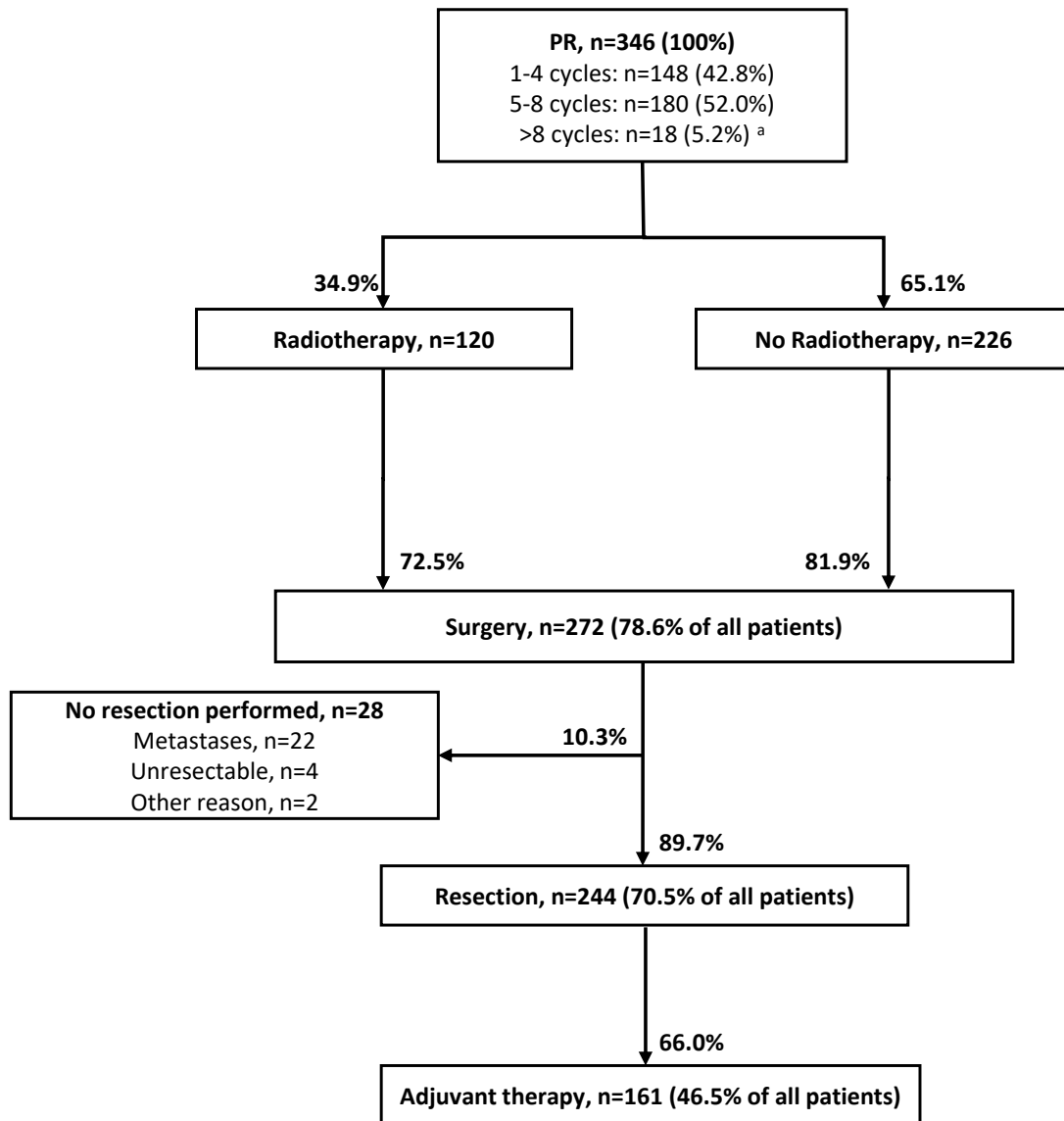
<sup>a</sup> = 126 patients (13%) also received second chemotherapy. LA = locally advanced.

B)



<sup>a</sup> = 77 patients (15%) also received second chemotherapy. BR = borderline resectable.

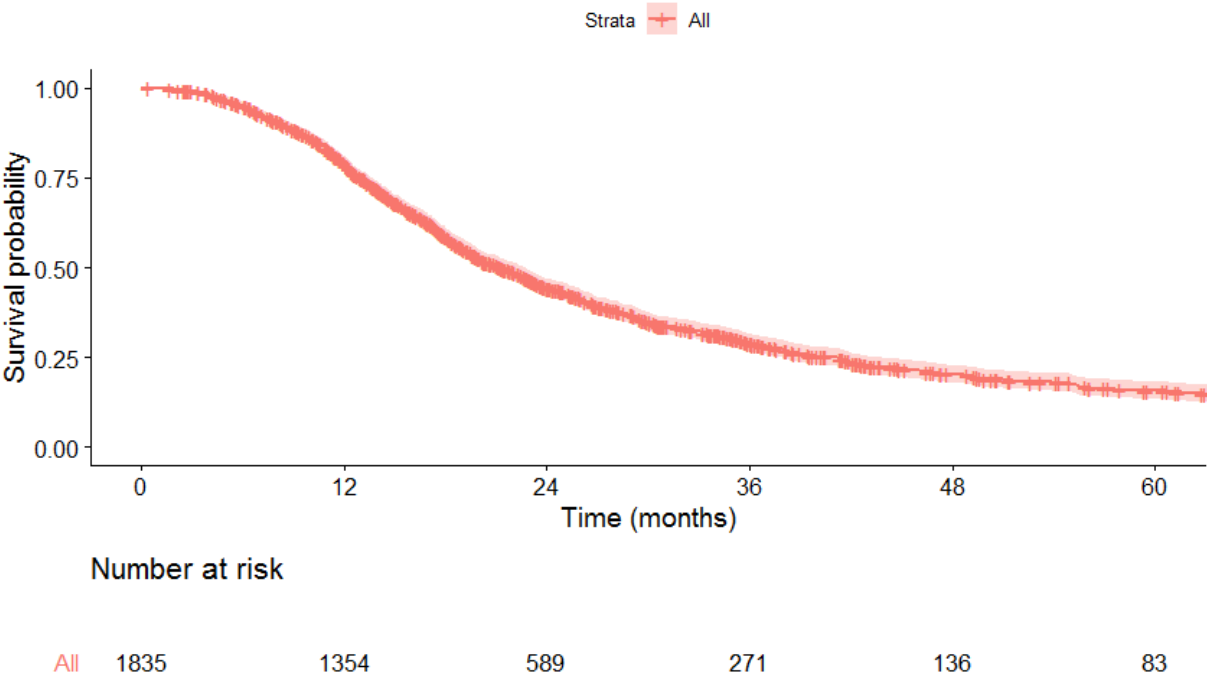
c)



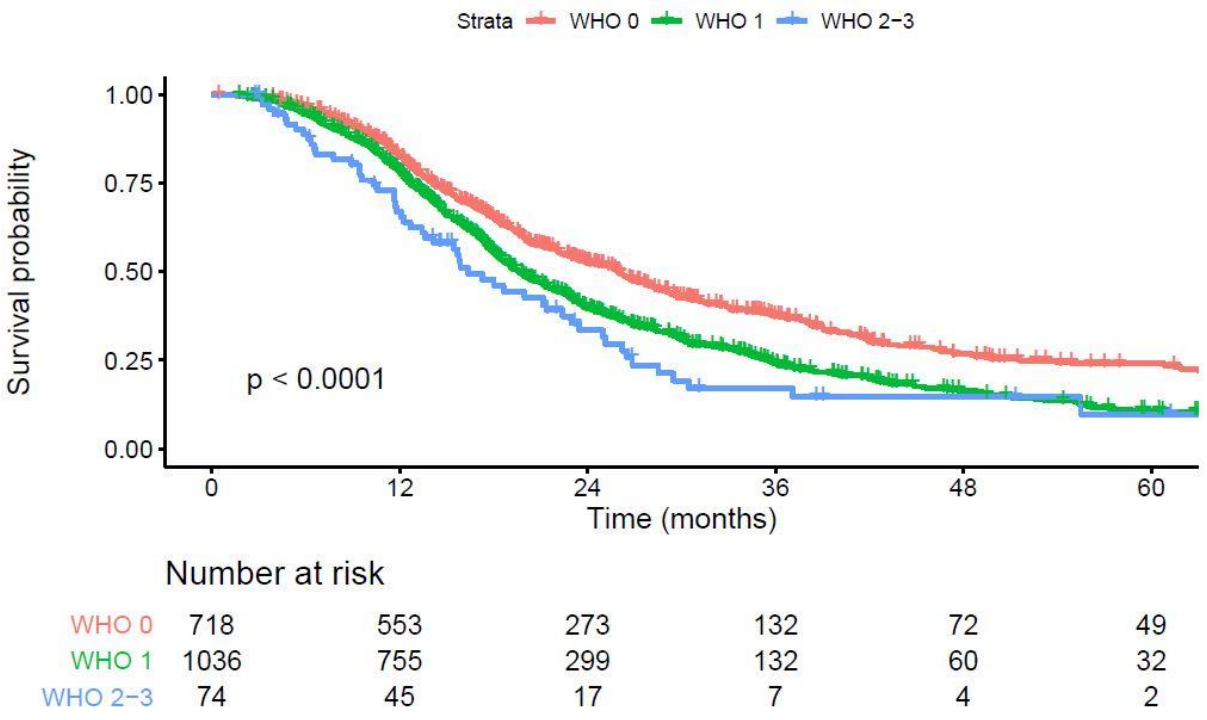
<sup>a</sup> = 33 patients (10%) also received second chemotherapy. PR = potentially resectable.

**Supplementary Figure 2. Overall survival of all patients with localized pancreatic adenocarcinoma treated with (m)FOLFIRINOX as initial treatment, by World Health Organization (WHO) performance status, by Body Mass Index (BMI), and by Carbohydrate Antigen (CA) 19-9 level in U/mL prior to start of (m)FOLFIRINOX treatment.**

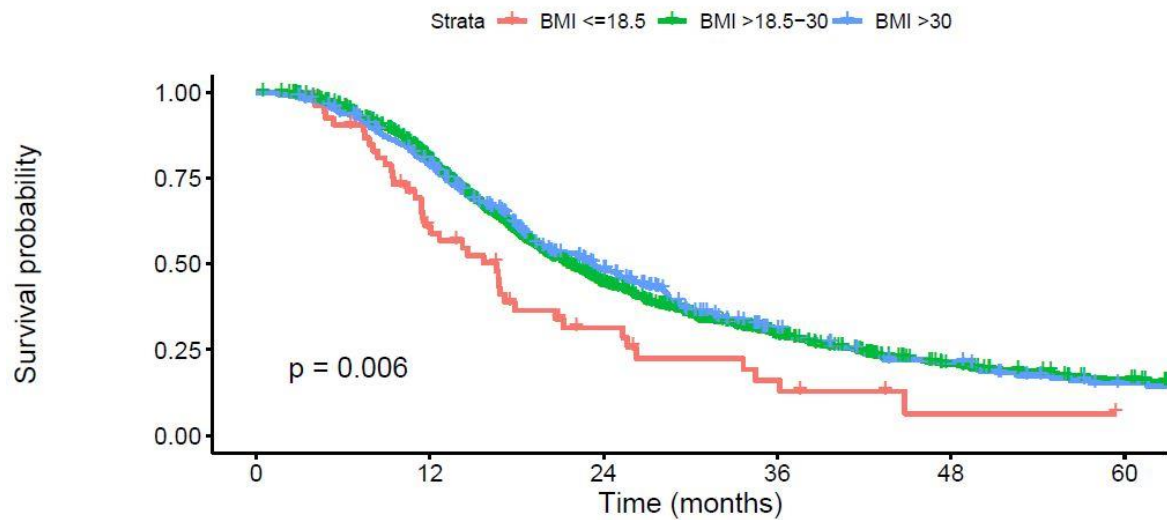
**A)**



**B)**



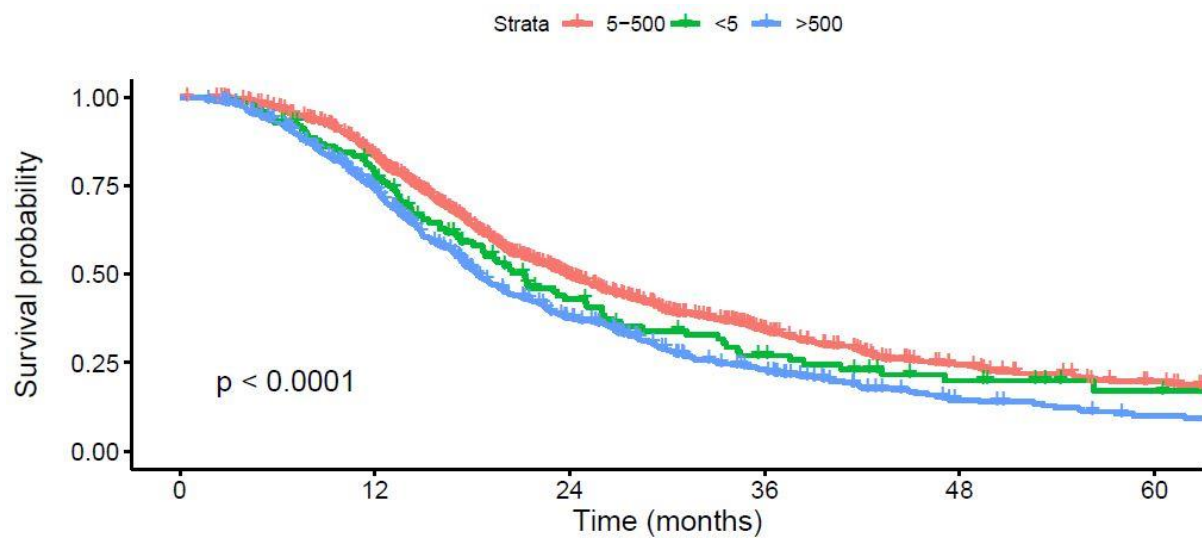
**C)**



Number at risk

	0	12	24	36	48	60
BMI <=18.5	53	29	11	5	1	0
BMI >18.5-30	1374	1025	438	208	100	66
BMI >30	387	289	137	57	35	17

D)



Number at risk

	0	12	24	36	48	60
5-500	1016	798	357	164	89	57
<5	124	93	40	22	12	6
>500	559	378	154	71	28	16

Difference in survival outcomes between groups was tested using the log-rank test. All tests were 2-sided.