Supplemental Online Content

Huffman BM, Basu Mallick A, Horick NK, et al. Effect of a MUC5AC antibody (NPC-1C) administered with second-line gemcitabine and nab-paclitaxel on the survival of patients with advanced pancreatic ductal adenocarcinoma: a randomized clinical trial. *JAMA Netw Open.* 2023;6(1):e2249720. doi:10.1001/jamanetworkopen.2022.49720

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1: NPC-1C staining score

NPC1C staining score (% tumor cells stained)	N (%)
20-40	35 (44.8%)
41-60	17 (21.8%)
61-80	14 (17.9%)
81-100	12 (15.4%)

eTable 2: Best Radiological Response According to RECIST Criteria

Response	Gemcitabine/nab-Paclitaxel/NPC-1C (N=32)	Gemcitabine/nab-Paclitaxel (N=34)	All Patients (N=66)
Complete Response	0	0	0
Partial Response	1 (3%, 95% CI: 0.4%-20%)	1 (3%, 95% CI: 0.4%-19%)	2 (3%, 95% CI: 0.7%-12%)
Stable Disease for >16 weeks	8 (25%, 95% CI: 13%-43%)	7 (21%, 95% CI: 10%-38%)	15 (23%, 95% CI: 14%-35%)
Stable Disease for < 16 weeks	4 (13%, 95% CI: 5%-29%)	7 (21%, 95% CI: 10-38%)	11 (17%, 95% CI: 9%-28%)
Progressive Disease	19 (59%, 95% CI: 42%-75%)	19 (56%, 95% CI: 39%-72%)	38 (58%, 95% CI: 45%-69%)

eTable 3: Frequency of Adverse Events by Grade That Were Possibly, Probably, or Definitely Related to Protocol Treatment

Grade of Toxicity	Gemcitabine/nab-paclitaxel/NPC-1C (n=38)	Gemcitabine/nab-paclitaxel alone (N=40)	p value (Fisher exact test)
Any grade toxicity	38 (100%)	40 (100%)	1
Grade ≥3 toxicity	27 (78%)	34 (85%)	0.17

eTable 4: Grade 3 or 4 Adverse Events Possibly, Probably, or Definitely Associated with Protocol Treatment

All Grade ≥3 Events	All Patients (n=78)	Gemcitabine/nab-paclitaxel/NPC-1C (n=38)	Gemcitabine/nab-paclitaxel (n=40)	P value[a]
Abdominal Pain	1 (1%)	1 (3%)	0 (0%)	0.49
Anemia	19 (24%)	15 (39%)	4 (10%)	0.003
Anorexia	1 (1%)	1 (3%)	0 (0%)	0.49
Coagulopathy	1 (1%)	0 (0%)	1 (3%)	1.0
Colitis	1 (1%)	1 (3%)	0 (0%)	0.49
Dehydration	1 (1%)	1 (3%)	0 (0%)	0.49
Diarrhea	1 (1%)	0 (0%)	1 (3%)	1.0
Edema	1 (1%)	0 (0%)	1 (3%)	1.0
Fatigue	6 (8%)	5 (13%)	1 (3%)	0.1
Fever	1 (1%)	1 (3%)	0 (0%)	0.49
Hyperglycemia	1 (1%)	0 (0%)	1 (3%)	1.0
Hypertension	1 (1%)	1 (3%)	0 (0%)	0.49
Hyponatremia	1 (1%)	0 (0%)	1 (3%)	1.0
Hypophosphatemia	2 (3%)	1 (3%)	1 (3%)	1.0
Leukopenia	13 (17%)	8 (21%)	5 (13%)	0.37
Abnormal liver function test	8 (10%)	6 (16%)	2 (5%)	0.15
Lymphopenia	6 (8%)	3 (8%)	3 (8%)	1.0
Mucositis	1 (1%)	0 (0%)	1 (3%)	1.0
Nausea	1 (1%)	0 (0%)	1 (3%)	1.0
Neutropenia	26 (33%)	14 (37%)	12 (30%)	0.63
Pancytopenia	2 (3%)	1 (3%)	1 (3%)	1.0
Peripheral Neuropathy	4 (5%)	1 (3%)	3 (8%)	0.62
Pneumonitis	1 (1%)	1 (3%)	0 (0%)	0.49
Rectal hemorrhage	1 (1%)	0 (0%)	1 (3%)	1.0
Thrombocytopenia	20 (26%)	12 (32%)	8 (20%)	0.3
Urinary tract infection	1 (1%)	0 (0%)	1 (3%)	1.0
Viral pharyngitis	1 (1%)	0 (0%)	1 (3%)	1.0

[a] P value calculated from Fisher's exact test comparing Gemcitabine/nab-paclitaxel/NPC-1C to Gemcitabine/nab-paclitaxel.

eTable 5: Relative Treatment Dose Intensity (RTDI)

Gemcitabine dosing	**All patients**	**Gemcitabine/nab-paclitaxel**	**Gemcitabine/nab-paclitaxel/NPC-1C**	**P value (Wilcoxon-Mann-Whitney test)**
Mean RTDI[a]	73.4 (95% CI: 69.3-77.6)	75.2 (95% CI: 68.8-81.6)	72.4 (95% CI: 66.1-77.2)	0.37
Median RTDI (Q1-Q3)	69.7 (33-100)	72.26 (49-100)	68.9 (47-100)	
Nab-paclitaxel dosing				
Mean RTDI	73.6 (95% CI: 69.3-77.9)	75.3 (95% CI: 68.9-81.7)	71.8 (95% CI: 65.9-77.7)	0.42
Median RTDI (Q1-Q3)	69.7 (33-100)	73.3 (48.9-100)	68.9 (46.7-100)	

[a] The relative treatment dose intensity (RTDI) of gemcitabine and nab-paclitaxel was calculated as the ratio of the actual cumulative chemotherapy dose to the protocol-specified cumulative dose. The protocol-specified cumulative dose was calculated by looking at the protocol defined dose for patients completing three cycles of therapy. For patients who discontinued the trial before cycle 3, the protocol specified dose was defined by the cycle that the patient came off the study.

eTable 6: Chemotherapy Dose Reductions

Gemcitabine/Nab-paclitaxel/NPC-1C Arm				
	All Cycles (n=38)	Cycle 1 (n=38)	Cycle 2 (n=33)	Cycle 3 (n=18)
Gemcitabine				
800 mg/m2	19 (50%)	18 (47%)	12 (36%)	6 (33%)
600 mg/m2	9 (24%)	2 (5%)	5 (15%)	5 (28%)
Nab-paclitaxel				
100 mg/m2	16 (42%)	17 (45%)	11 (33%)	4 (24%)
75 mg/m2	11 (29%)	2 (5%)	5 (15%)	6 (35%)
Held	0 (0%)	0 (0%)	0 (0%)	1 (6%)
Gemcitabine/Nab-paclitaxel Arm				
	All Cycles (n=40)	Cycle 1 (n=40)	Cycle 2 (n=32)	Cycle 3 (n=20)
Gemcitabine				
800 mg/m2	16 (40%)	12 (30%)	10 (31%)	5 (25%)
600 mg/m2	9 (23%)	4 (10%)	4 (13%)	4 (20%)
Nab-paclitaxel				
100 mg/m2	15 (38%)	12 (30%)	9 (29%)	4 (22%)
75 mg/m2	10 (25%)	4 (10%)	3 (10%)	5 (28%)
Held	0 (0%)	0 (0%)	1 (3%)	2 (10%)
P values[a] (Gemcitabine/nab-paclitaxel)	0.54/0.74	0.33/0.41	0.84/0.78	0.65/0.91
[a] P values compared difference in dose reductions of each drug between the two arms				

eTable 7: Modifications of Chemotherapy Administration Schedule

Gemcitabine/Nab-paclitaxel/NPC-1C Arm				
	All Cycles (n=38)	Cycle 1 (n=38)	Cycle 2 (n=33)	Cycle 3 (n=18)
Continue 3 weeks on/ 1 week off (N,%)	9 (23.7%)	18 (47.4%)	15 (45.5%)	9 (50%)
2 weeks on/ 2 weeks off (N, %)	10 (26.3%)	7 (18.4%)	9 (27.3%)	5 (27.8%)
1 week on/1 week off (N,%)	15 (39.5%)	12 (31.6%)	6 (18.2%)	4 (22.2%)
1 week on/3 weeks off (N,%)	4 (10.5%)	1 (2.6%)	3 (9.1%)	0 (0%)
Gemcitabine/Nab-paclitaxel Arm				
	All Cycles (n=40)	Cycle 1 (n=40)	Cycle 2 (n=32)	Cycle 3 (n=20)
Continue 3 weeks on/ 1 week off (N,%)	14 (35%)	26 (65%)	20 (62.5%)	7 (35%)
2 weeks on/2 weeks off (N, %)	10 (25%)	7 (17.5%)	8 (25%)	4 (20%)
1 week on/1 week off (N,%)	6 (15%)	3 (7.5%)	3 (9.4%)	4 (20%)
1 week on/3 weeks off (N,%)	10 (25%)	4 (10%)	1 (3.1%)	5 (25%)
P value between treatment arms (Fisher exact test)	0.06	0.03	0.46	0.15

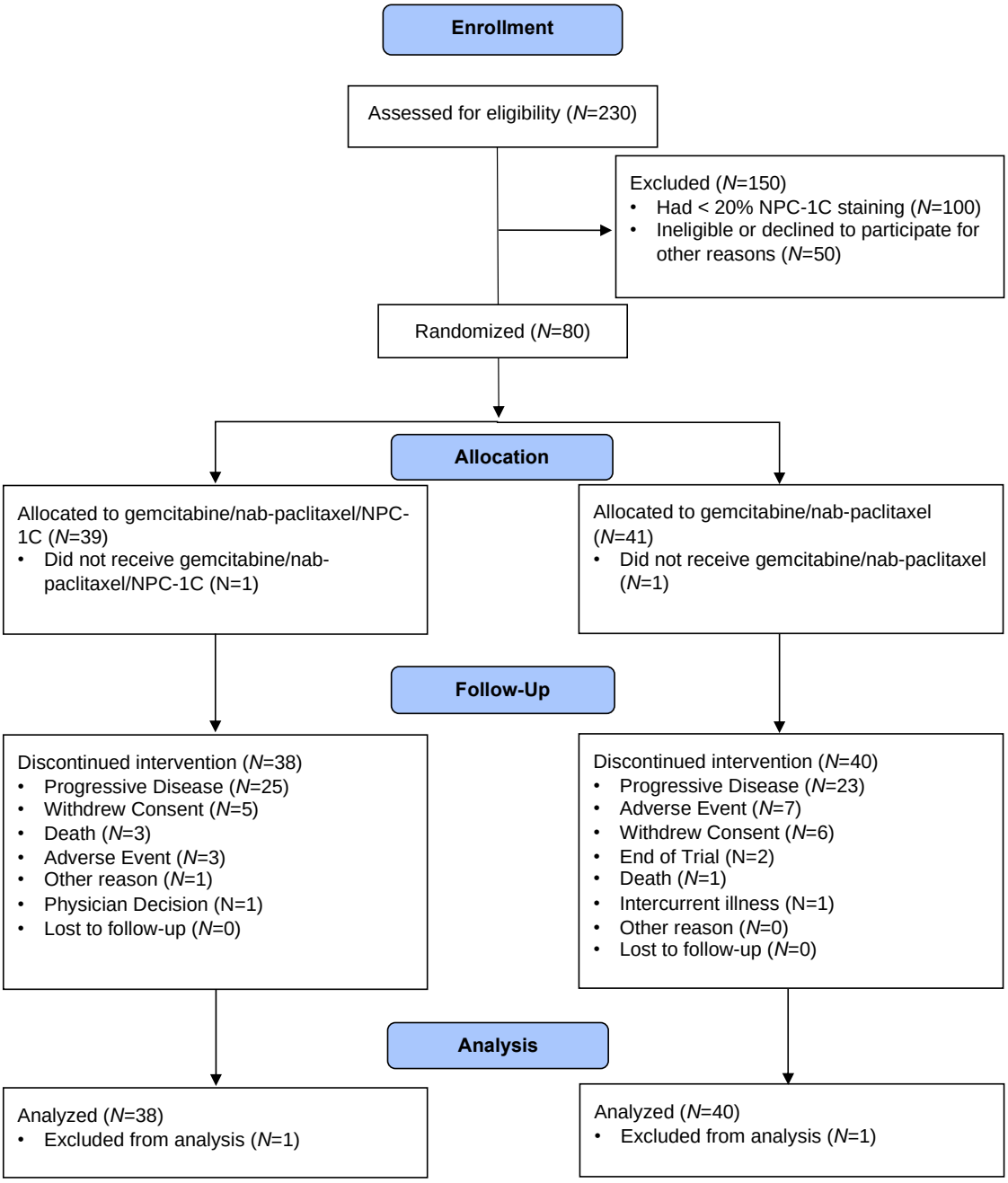
eTable 8: Univariate analysis of Prognostic Features Associated with Overall Survival

Characteristic	Reference	Comparator	Hazard Ratio	95% Confidence Interval	p value
Treatment	Gemcitabine/ nab-paclitaxel	Gemcitabine/ nab-paclitaxel/ NPC-1C	1.34	0.84-2.13	0.2252
Age	Age < 50 years	Age ≥ 50 years	1.07	0.51-2.23	0.8642
Sex	Male	Female	1.06	0.66-1.72	0.7999
ECOG performance status	0	1	1.24	0.76-2.02	0.3947
Stage	Locally advanced	Metastatic	1.34	0.49-3.71	0.5683
Two or more sites of metastatic disease	No	Yes	1.92	1.18-3.12	0.0082
Surgery and/or radiation	No	Yes	0.56	0.34-0.92	0.0231
Time from diagnosis to trial treatment	≤ 18 months	>18 months	1.46	0.86-2.48	0.1659
Lymphocyte-to-monocyte ratio < 2.8	No	Yes	1.92	0.92-3.92	0.0801
CA19-9 > 2000 IU/mL	No	Yes	1.94	1.20-3.14	0.0067
Albumin < 3.4 g/dL	No	Yes	3.70	1.87-7.31	0.0002
Neuropathy	No	Yes	0.70	0.44	1.12
Diabetes mellitus	No	Yes	1.47	0.88-2.45	0.1461
Liver metastases	No	Yes	2.64	1.49-4.67	0.0009
Pulmonary metastases	No	Yes	0.70	0.37-1.30	0.2602
Peritoneal metastases	No	Yes	1.14	0.65-2.00	0.6389
NPC-1C staining score[a]	< 50%	≥ 50%	1.16	0.72-1.86	0.5406
Neutrophil-to-lymphocyte ratio ≥ 5	No	Yes	1.73	1.05-2.85	0.0300
Platelet-to-lymphocyte ratio ≥ 180	No	Yes	1.50	0.91-2.47	0.1155

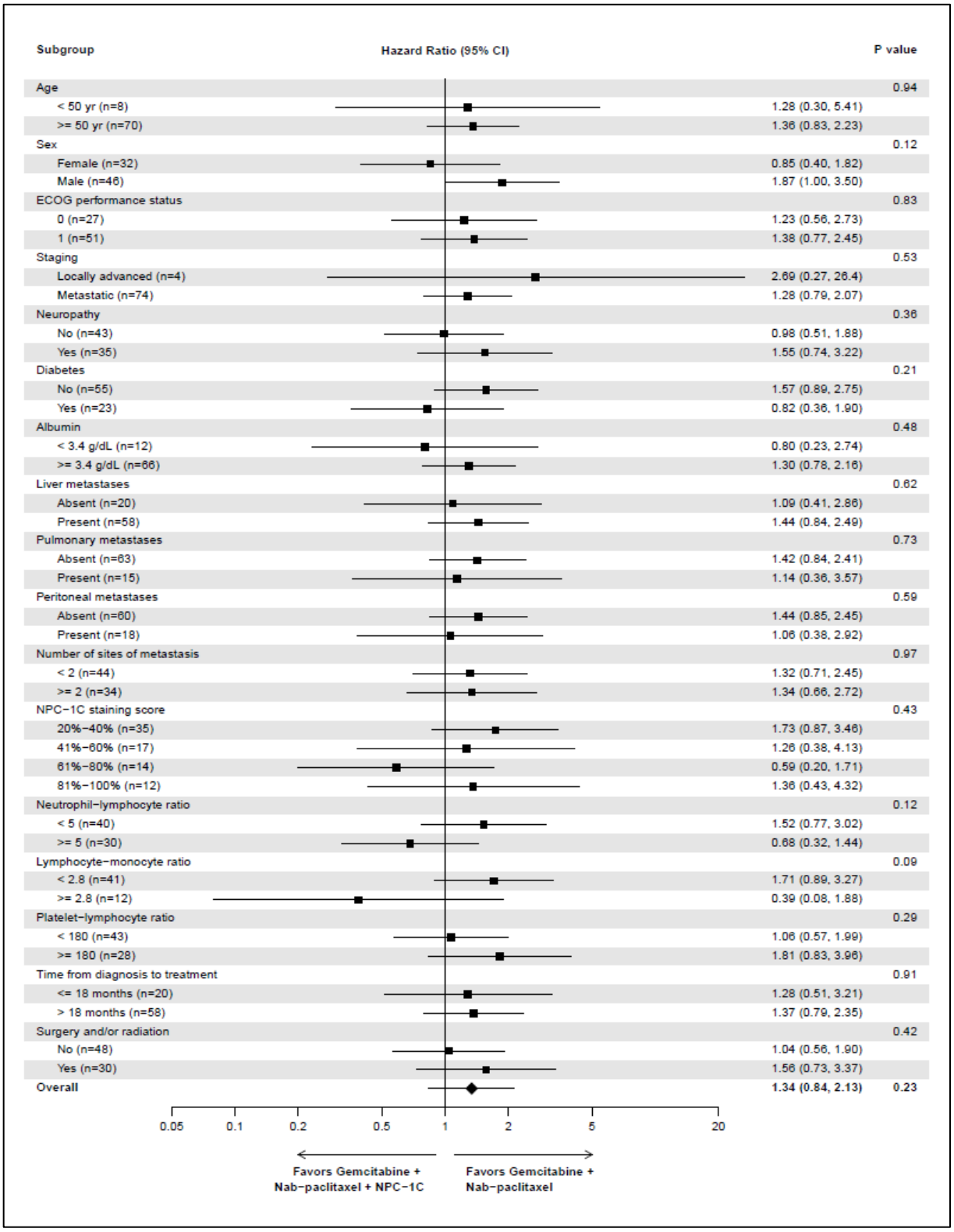
[a] NPC-1C staining score was obtained via centralized immunohistochemical analysis.

ECOG: Eastern Cooperative Oncology Group; IU/mL: International Units/milliliter; g/dL: grams/deciliter

eFigure 1: CONSORT Diagram for Patient Disposition



eFigure 2: Subgroup Analysis of Demographic and Baseline Disease Characteristics in Relation to Overall Survival



eFigure 3: Overall Survival of Patients Based on Presence of Prognostic Factors