

Supplemental Online Content

Raghavendra AS, Bassett R Jr, Damodaran S, et al. Clinical characteristics and survival outcomes of metastatic invasive lobular and ductal carcinoma. *JAMA Netw Open*. 2025;8(3):e251888. doi:10.1001/jamanetworkopen.2025.1888

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

eTable 1: Multivariate Model Results for Progression-Free Survival (PFS) and Overall Survival (OS)

Variable	Level	PFS		OS	
		HR (95% CI)	p-value	HR (95% CI)	p-value
Histology	Ductal		.049		.003
	Lobular	0.92 (0.85-1.00)		1.15 (1.05-1.26)	
Age at First Metastasis	Continuous	1.00 (0.99-1.00)	<.001	1.01 (1.00-1.01)	<.001
Number of Metastases	Continuous	1.08 (1.07-1.09)	<.001	1.08 (1.07-1.10)	<.001
Race	ASIAN/PACIFIC IS		.001		<.001
	BLACK	1.13 (0.99-1.30)		1.93 (1.63-2.30)	
	NATIVE AMERICAN	1.62 (0.91-2.89)		1.02 (0.48-2.17)	
	OTHER	1.22 (0.97-1.53)		1.43 (1.04-1.96)	
	SPANISH, HISPANIC	1.08 (0.94-1.23)		1.43 (1.20-1.70)	
	WHITE	0.99 (0.88-1.12)		1.41 (1.21-1.66)	
Site of Distant Metastasis	Non-visceral		<.001		<.001
	Visceral	1.15 (1.09-1.20)		1.43 (1.36-1.51)	
Timing of Metastasis	De Novo		.006		<.001
	Recurrent	0.93 (0.89-0.98)		1.56 (1.47-1.65)	
Subtype	HR+/HER2-		<.001		<.001
	HER2+	0.75 (0.70-0.79)		0.69 (0.64-0.74)	
	TNBC	1.60 (1.50-1.71)		1.77 (1.65-1.89)	
Nuclear Grade	I		<.001		<.001
	II	1.19 (1.04-1.35)		1.09 (0.94-1.27)	
	III	1.54 (1.35-1.76)		1.56 (1.34-1.82)	

eTable2: Disease-free interval (DFI) for each histologic group by estrogen receptor (ER) expression and tumor grade.

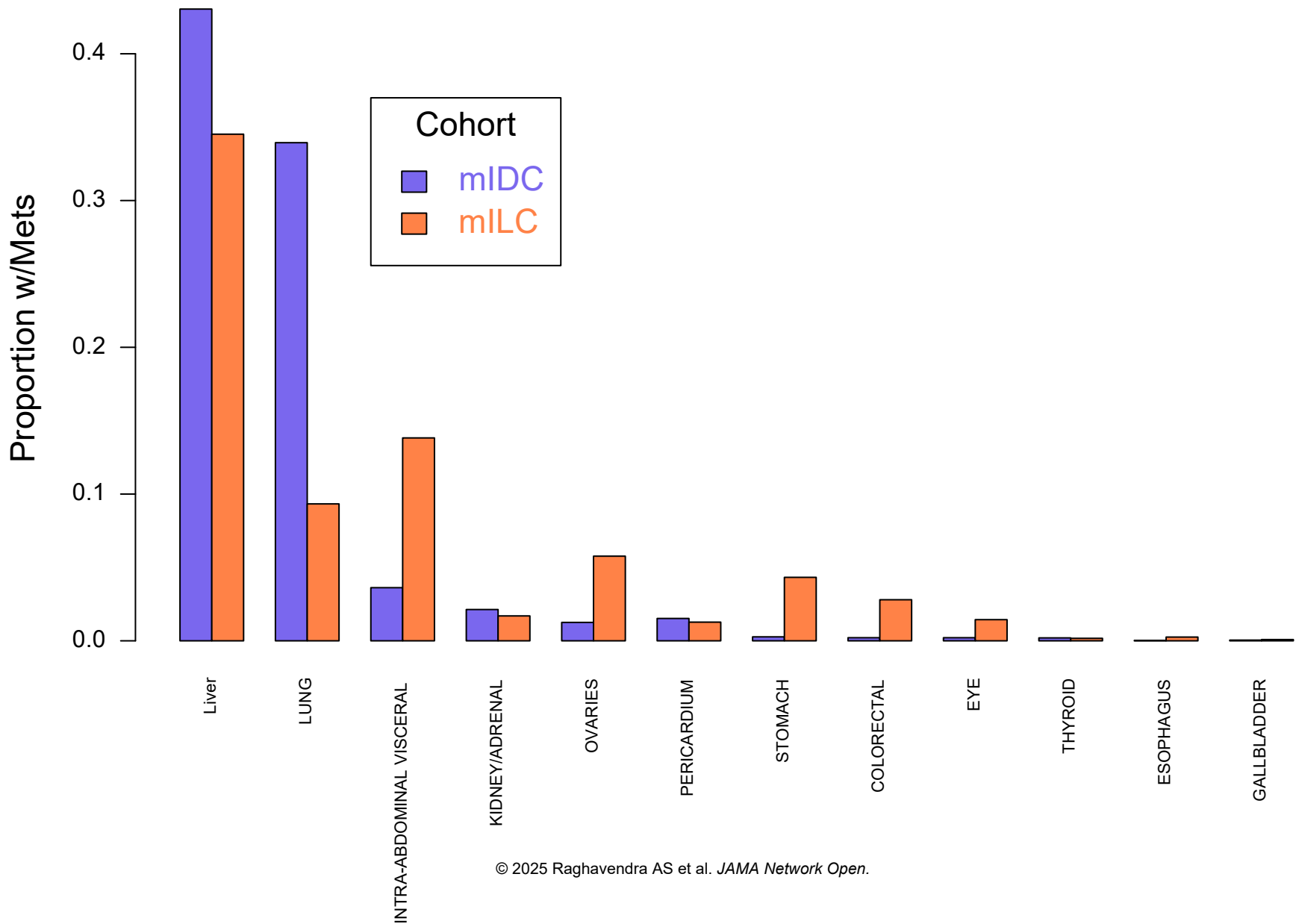
	mIDC		mILC		Hazard Ratio	P
	N	Median DFI (95% CI)	N	Median DFI (95% CI)		
Histologic group	6044	2.47 (2.39–2.55)	770	3.93 (3.56–4.26)	0.69	<.001
Subtype						
HR+/HER2-	3306	3.31 (3.21, 3.43)	672	4.14 (3.81, 4.47)	0.83	<.001
HER2+	1257	2.12 (1.99, 2.28)	48	3.01 (2.14, 4.32)	0.68	.005
TNBC	1481	1.53 (1.47, 1.60)	50	1.59 (1.25, 2.25)	0.68	.005
Tumor grade						
1	91	5.39 (4.31–6.63)	115	4.29 (3.74–5.57)	1.10	.51
2	1609	3.52 (3.38–3.66)	367	4.14 (3.64–4.60)	0.89	.046
3	3612	1.95 (1.89–2.02)	158	2.81 (2.03–3.07)	0.77	<.001

CI, confidence interval; mIDC, metastatic invasive ductal carcinoma; mILC, metastatic invasive lobular carcinoma.

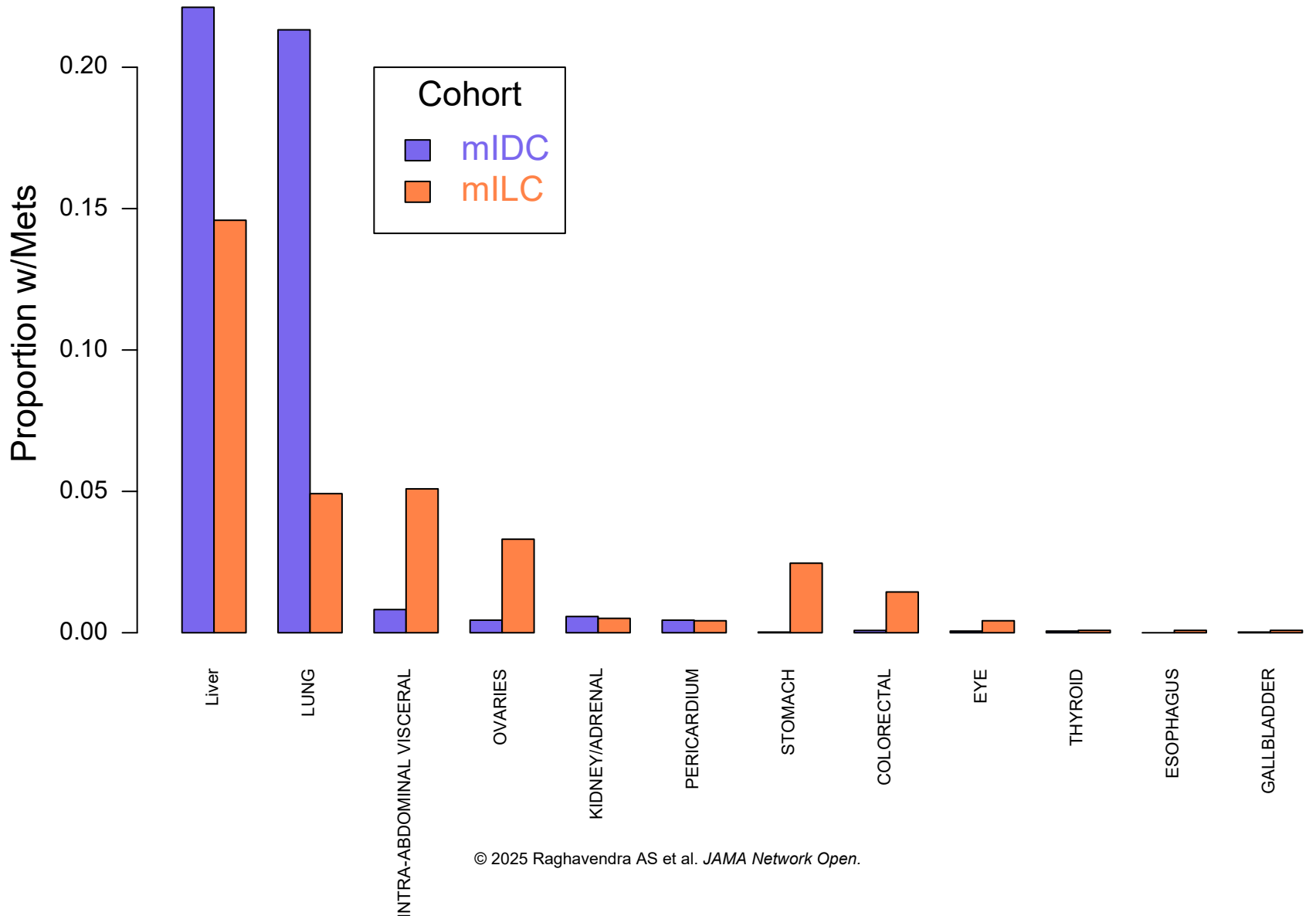
eTable 3. Key genomic alterations in patients with metastatic invasive ductal carcinoma (mIDC) and metastatic invasive lobular carcinoma (mILC) across subtypes.

Genomic Alteration	HR+HER2-mIDC, n (%)	HR+HER2-mILC, n (%)	HR+HER2- p-value	HER2+ mIDC, n (%)	HER2+ mILC, n (%)	HER2+ p-value	TNBC mIDC, n (%)	TNBC mILC, n (%)	TNBC p-value
Mutation									
<i>TP53</i>	294 (21.9%)	40 (13.9%)	.002	103 (27.2%)	4 (19.1%)	.61	234 (51.0%)	1 (4.8%)	<.001
<i>PIK3CA</i>	362 (27.0%)	109 (37.9%)	<.001	60 (15.8%)	4 (19.1%)	.76	59 (12.8%)	5 (23.8%)	.18
<i>ESR1</i>	137 (10.2%)	29 (10.1%)	1.00	13 (3.4%)	0 (0.0%)	1.00	9 (2.0%)	1 (4.8%)	.36
<i>NF1</i>	40 (3.0%)	19 (6.6%)	.005	9 (2.4%)	2 (9.5%)	.11	15 (3.3%)	1 (4.8%)	.52
<i>FGFR</i>	51 (3.8%)	12 (4.2%)	.74	6 (1.6%)	0 (0.0%)	1.00	12 (2.6%)	1 (4.8%)	.45
<i>RB1</i>	35 (2.6%)	10 (3.5%)	.43	7 (1.8%)	0 (0.0%)	1.00	22 (4.8%)	1 (4.8%)	1.00
<i>ERBB2</i>	33 (2.5%)	18 (6.2%)	.002	6 (1.6%)	4 (19.1%)	<.001	9 (2.0%)	0 (0.0%)	1.00
<i>AKT1</i>	32 (2.4%)	7 (2.4%)	1.00	8 (2.1%)	0 (0.0%)	1.00	9 (2.0%)	0 (0.0%)	1.00
<i>GATA3</i>	49 (3.7%)	1 (0.3%)	.001	7 (1.8%)	1 (4.8%)	0.35	3 (0.6%)	0 (0.0%)	1.00
<i>Cyclin E</i>	9 (0.7%)	1 (0.3%)	1.00	6 (1.6%)	0 (0.0%)	1.00	17 (3.7%)	0 (0.0%)	1.00
<i>Cyclin D</i>	22 (1.6%)	2 (0.7%)	.29	2 (0.5%)	0 (0.0%)	1.00	3 (0.6%)	0 (0.0%)	1.00
Amplification									
<i>Cyclin D</i>	104 (7.8%)	17 (5.9%)	.32	17 (4.5%)	1 (4.8%)	1.00	20 (4.4%)	0 (0.0%)	1.00
<i>FGFR</i>	79 (5.9%)	8 (2.8%)	.03	9 (2.4%)	0 (0.0%)	1.00	20 (4.4%)	0 (0.0%)	1.00

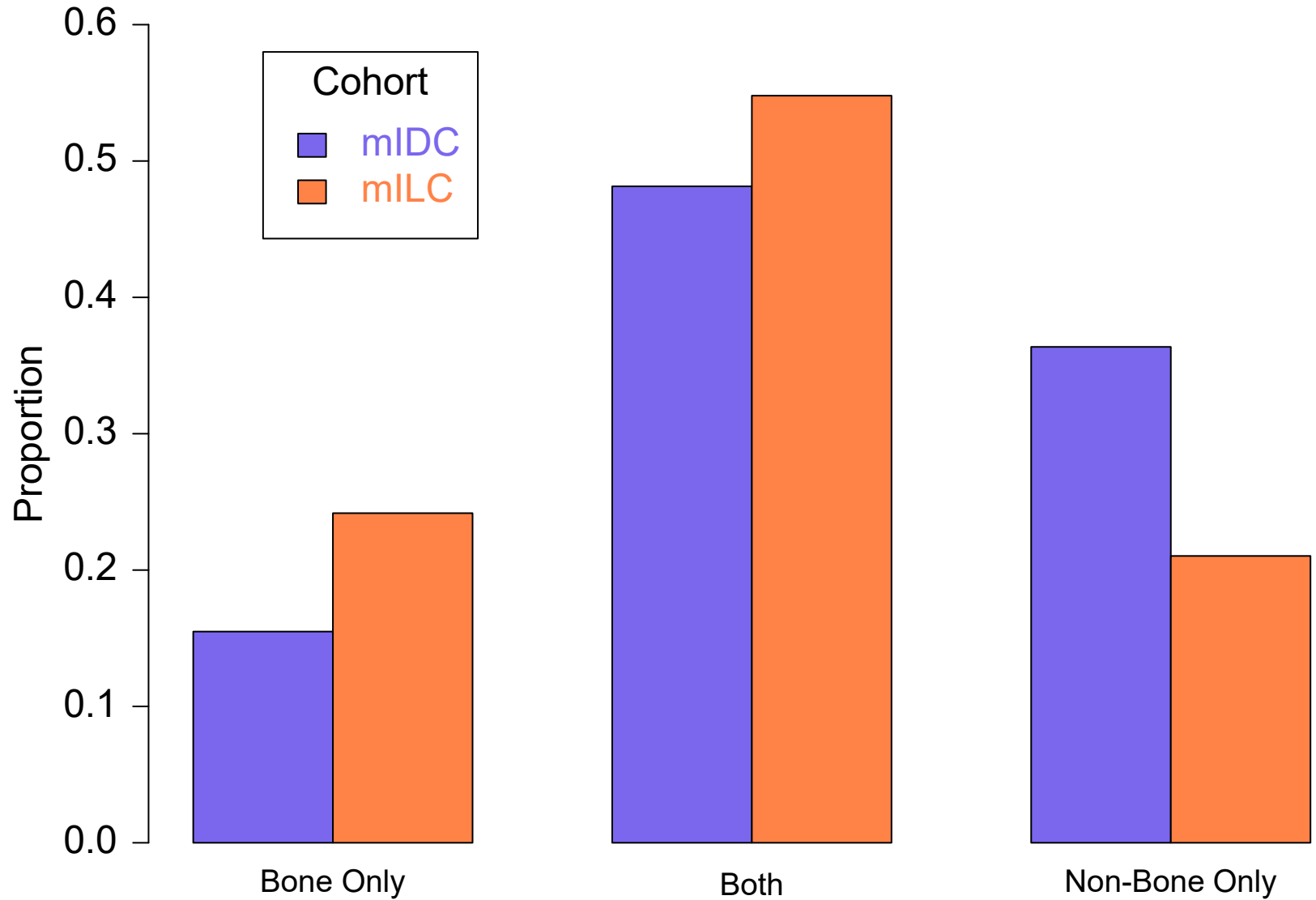
eFigure 1: Types of All Visceral Metastases



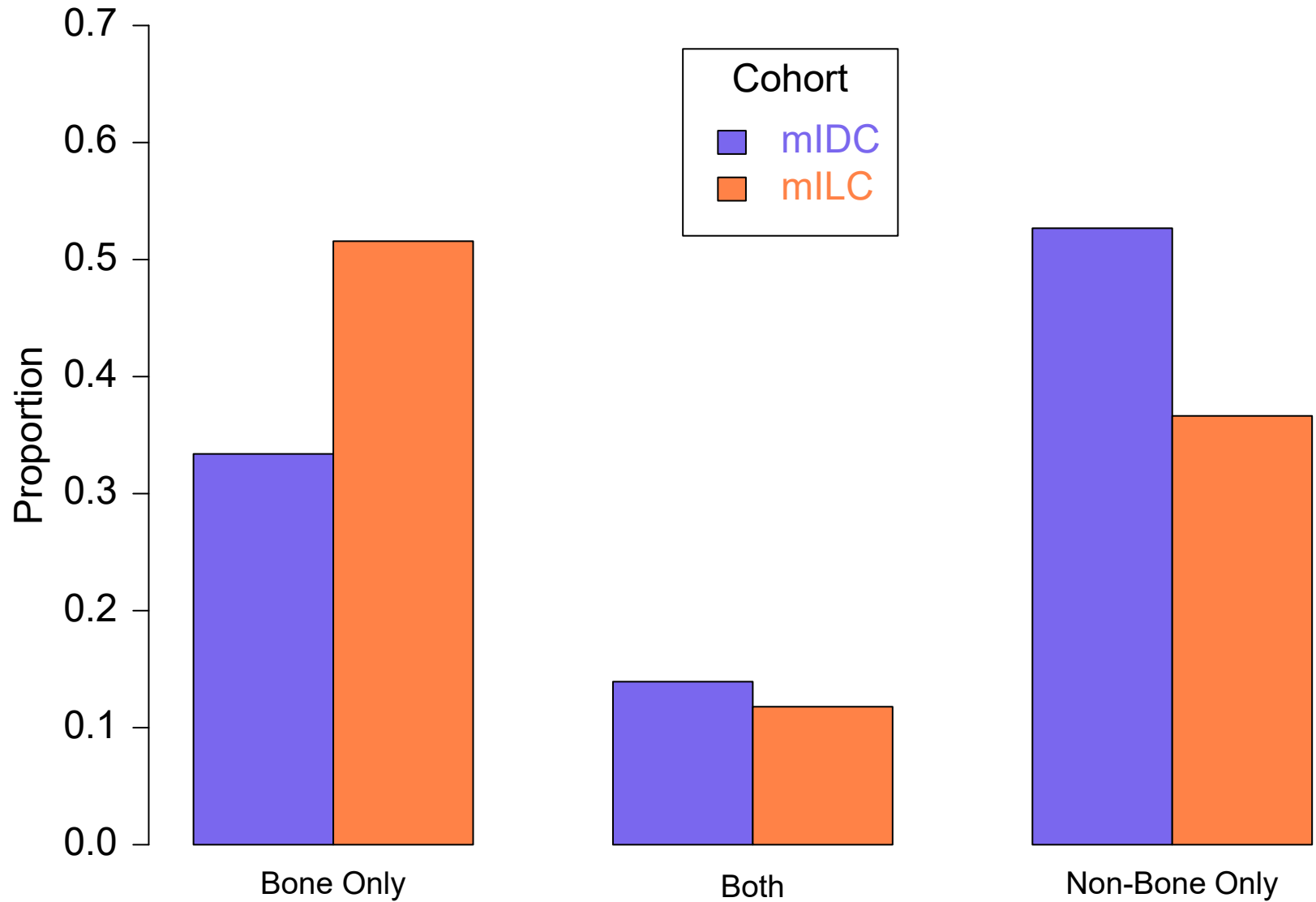
eFigure 2: Types of Visceral Metastases at Dx



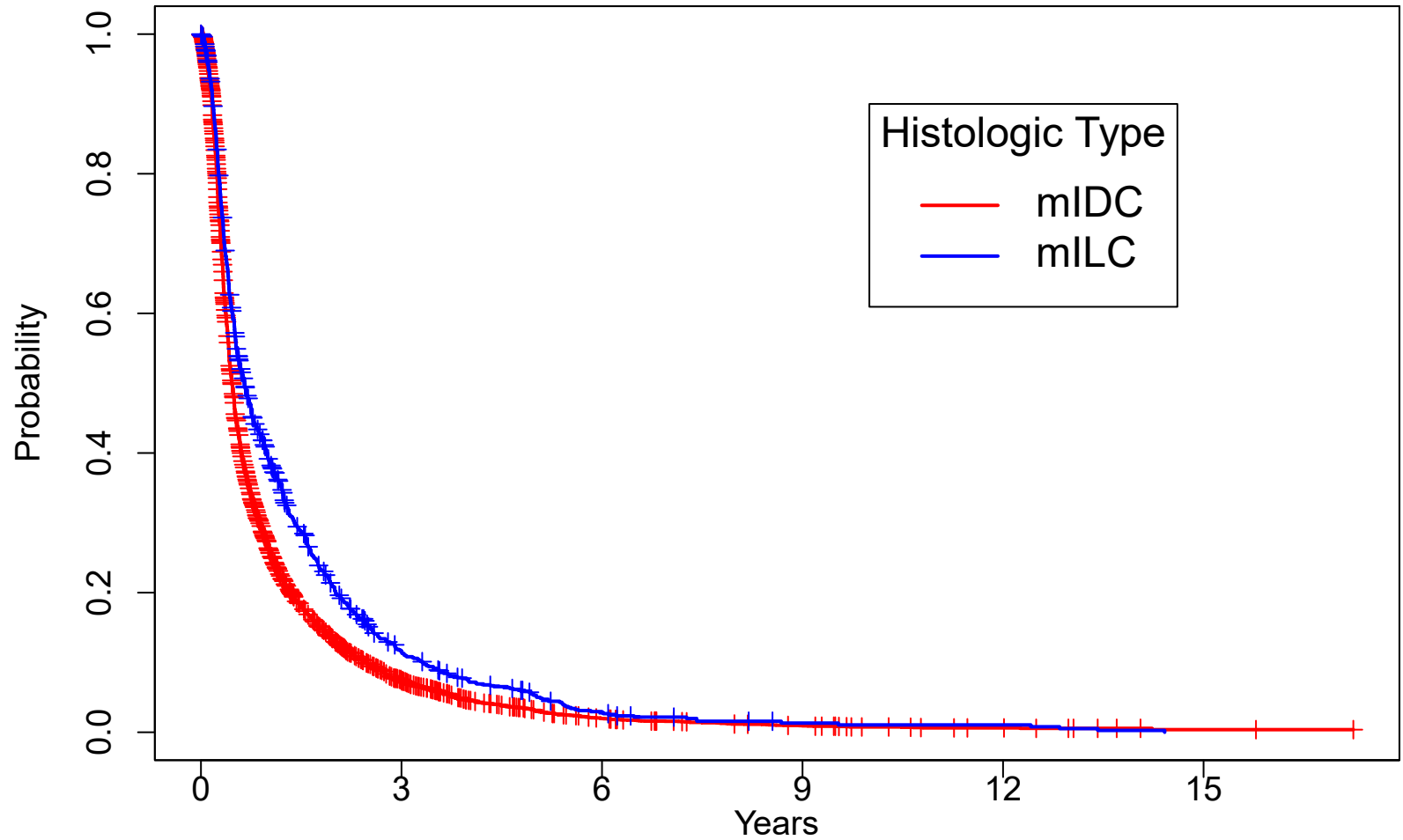
eFigure 3: Types of All Metastases



eFigure 4: Types of Metastasis at Dx



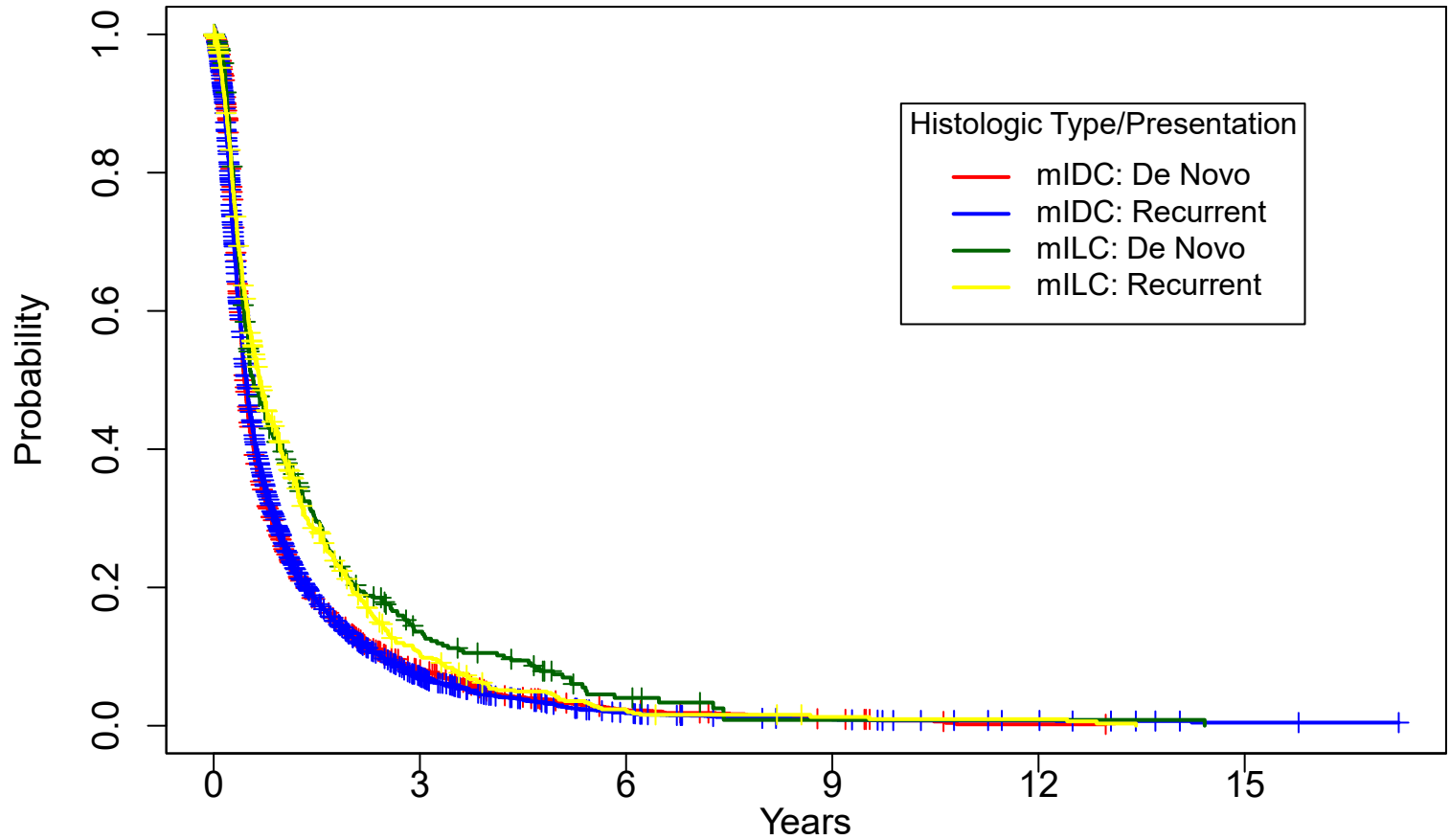
eFigure 5A: Progression-Free Survival by Histologic Type



N at risk

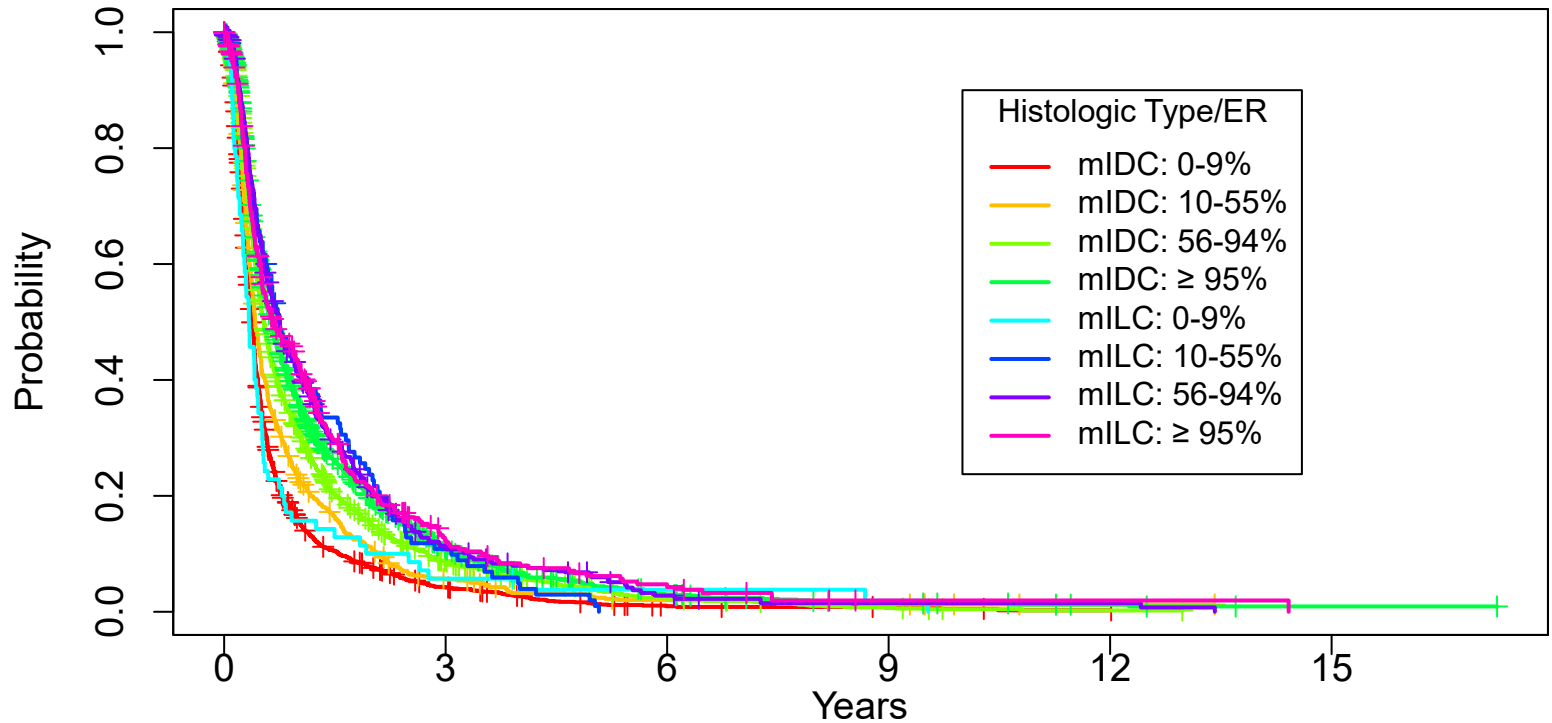
mIDC	7851	471	90	32	11	2
mILC	1089	99	19	5	4	0

eFigure 5B: Progression-Free Survival by Histologic Type and Presentation



N at risk		0	3	6	9	12	15
mIDC: De Novo	—	2407	159	32	11	1	
mIDC: Recurrent	—	5444	312	58	21	10	2
mILC: De Novo	—	389	40	8	1	1	
mILC: Recurrent	—	700	59	11	4	3	

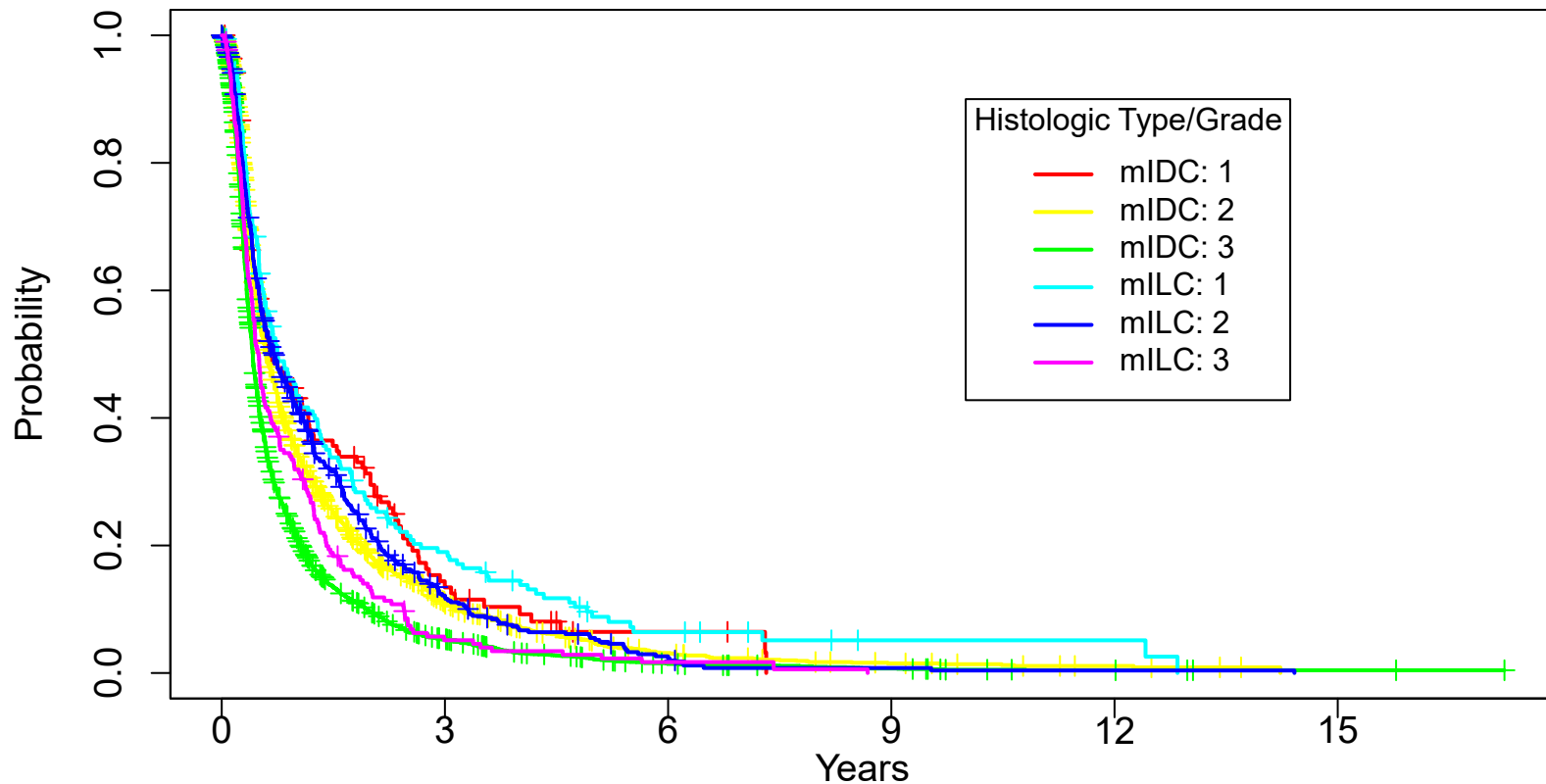
eFigure 5C: Progression-Free Survival by Histologic Type and ER Percent



N at risk

mIDC: 0-9%	1868	67	8	5	1	
mIDC: 10-55%	695	33	9	5	1	
mIDC: 56-94%	1967	138	28	7	1	
mIDC: ≥ 95%	2002	163	33	11	4	1
mILC: 0-9%	70	4	2	1		
mILC: 10-55%	106	11				
mILC: 56-94%	368	34	6	2	2	
mILC: ≥ 95%	367	31	9	1	1	

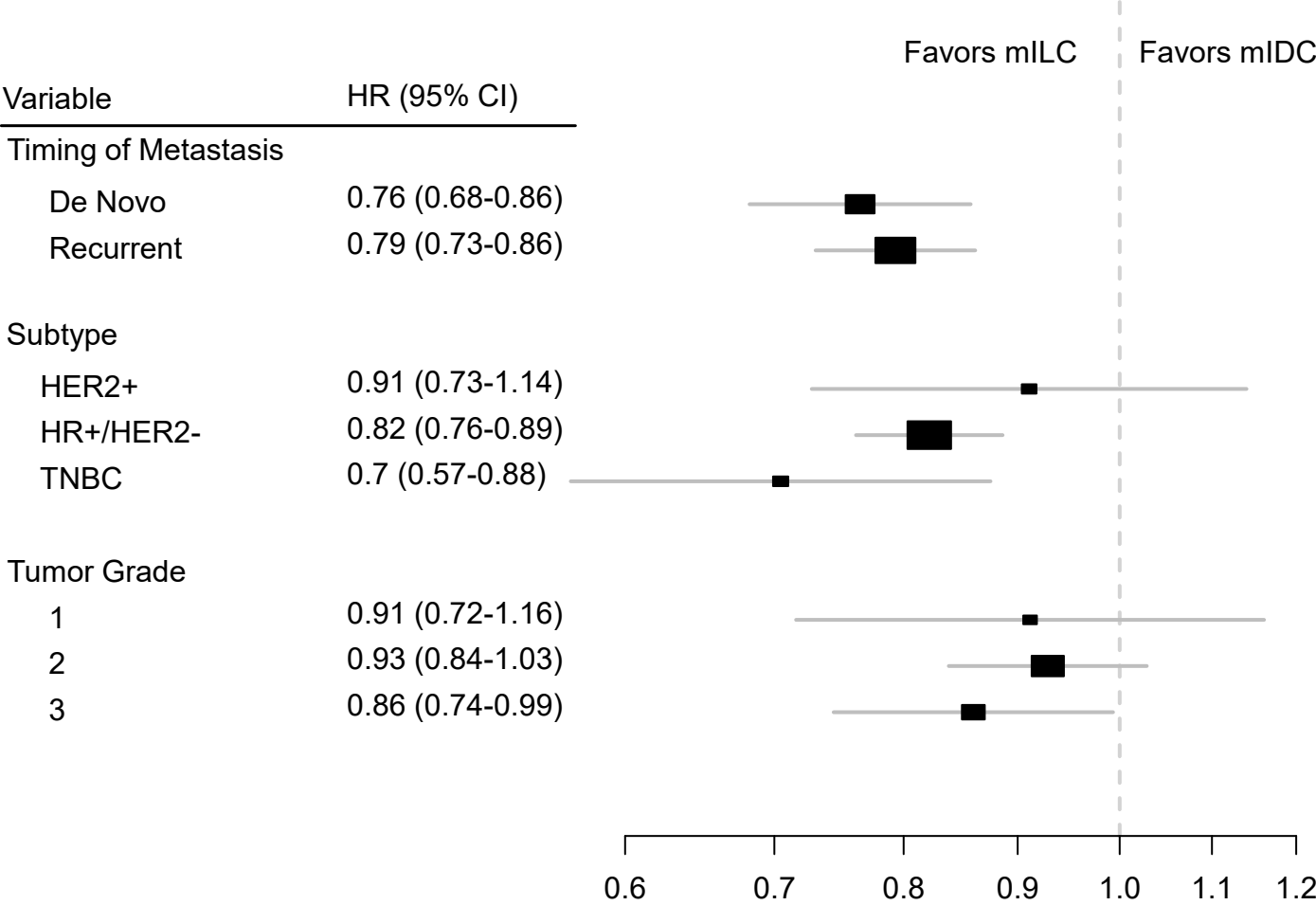
eFigure 5D: Progression-Free Survival by Histologic Type and Tumor Grade



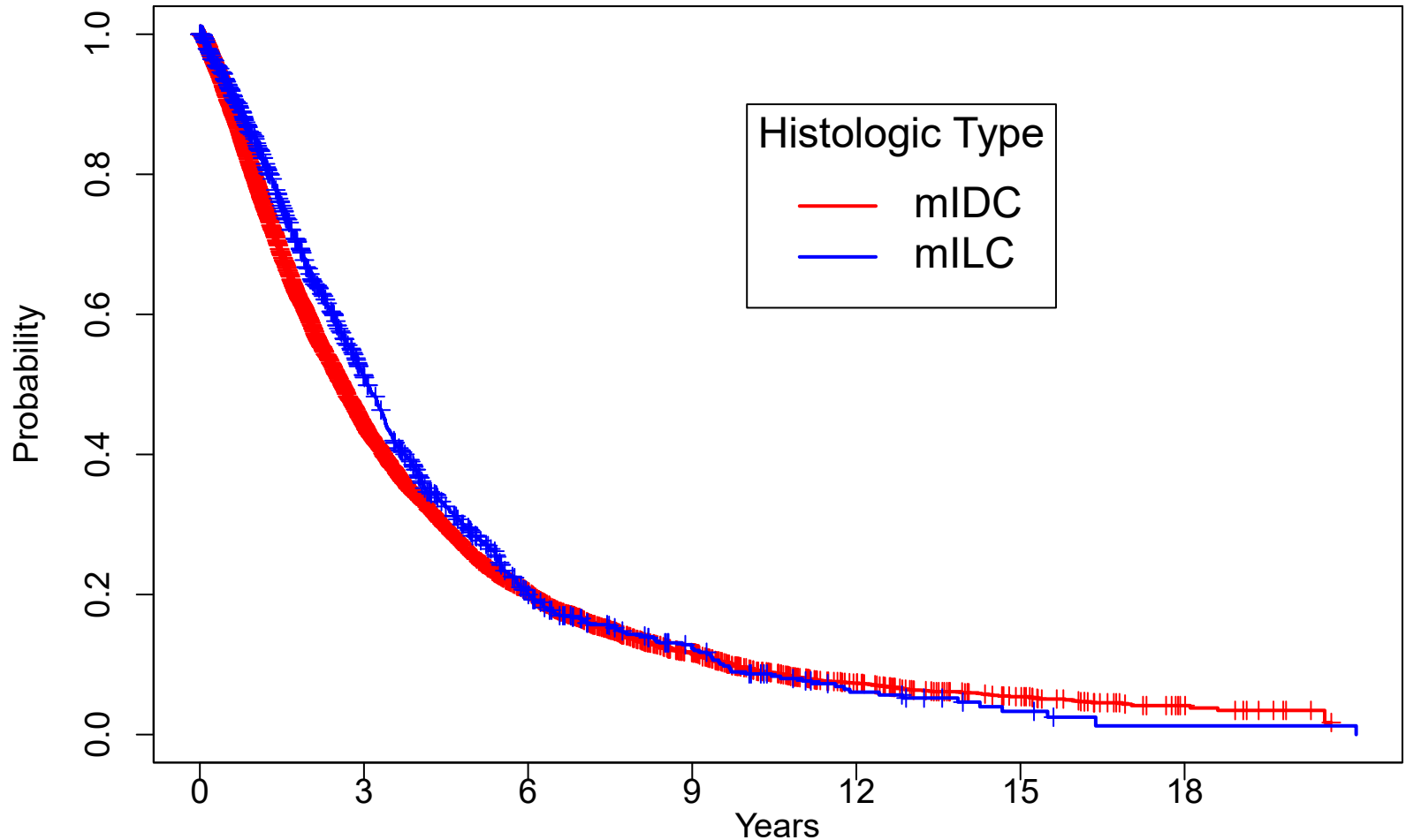
N at risk

mIDC: 1	141	14	3			
mIDC: 2	2220	192	41	14	5	
mIDC: 3	4485	206	41	17	5	2
mILC: 1	177	30	8	2	2	
mILC: 2	510	46	7	2	1	
mILC: 3	199	9	3			

eFigure 6: Forest Plot for PFS



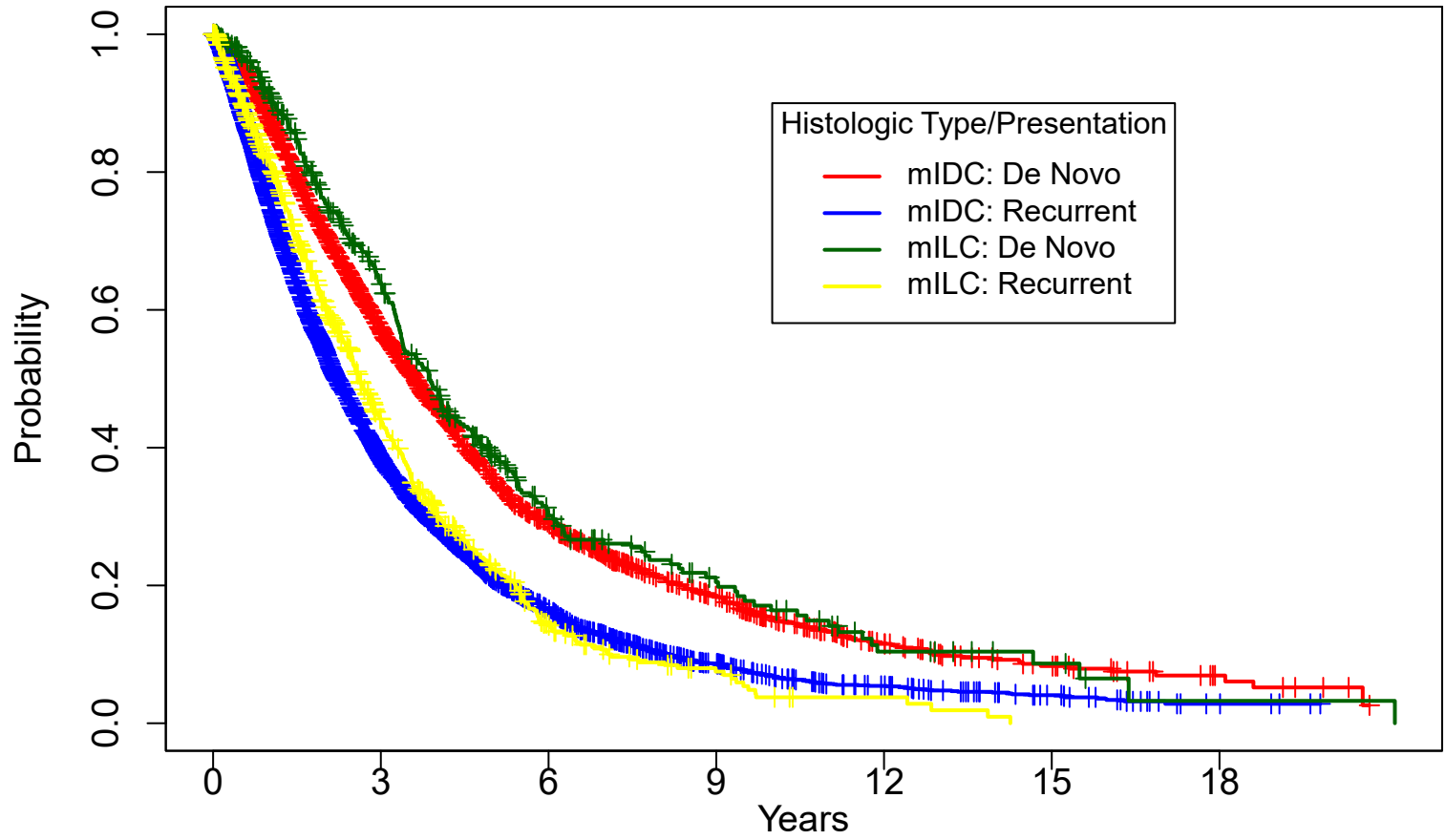
eFigure 7A: Overall Survival by Histologic Type



N at risk

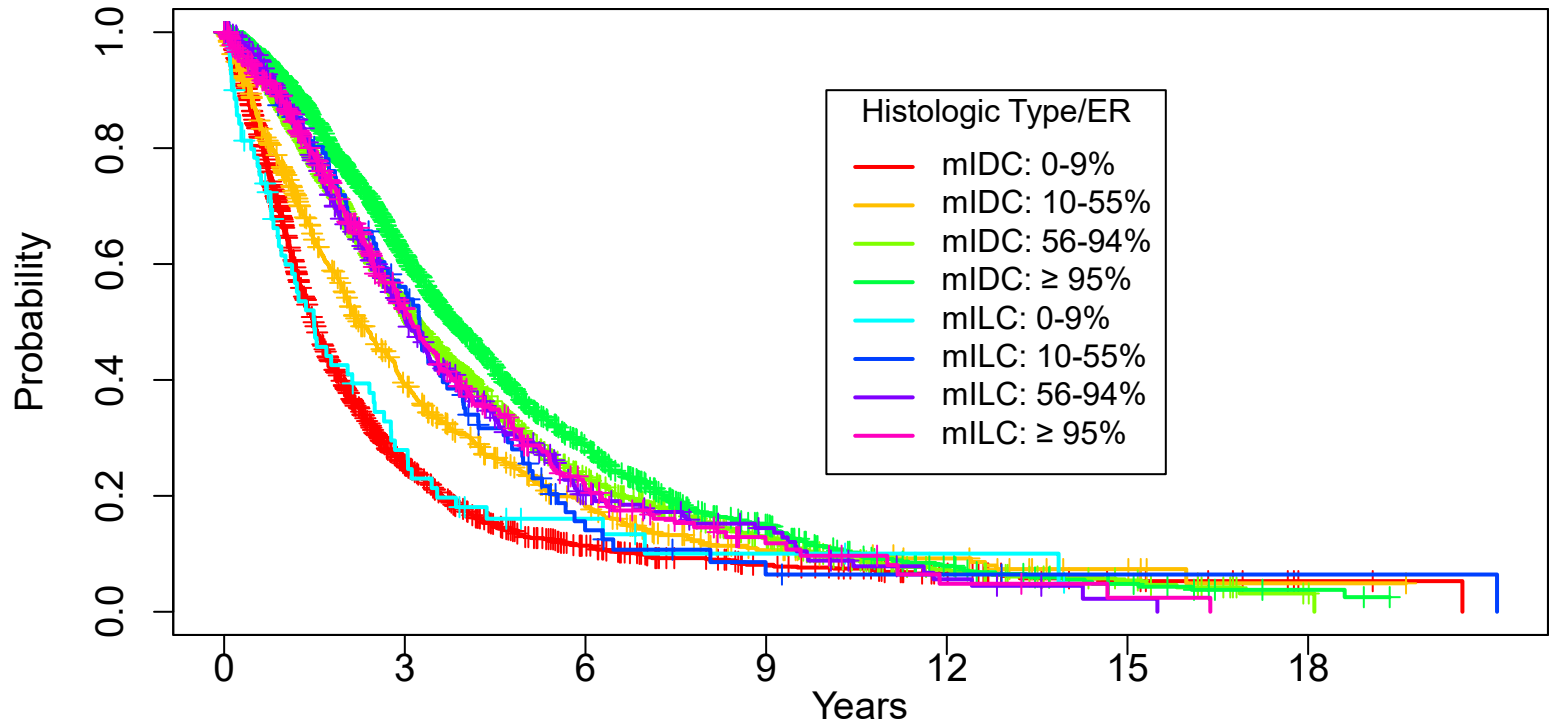
mIDC	7851	2673	902	347	131	54	13
mILC	1089	415	112	45	15	5	1

eFigure 7B: Overall Survival by Histologic Type and Presentation



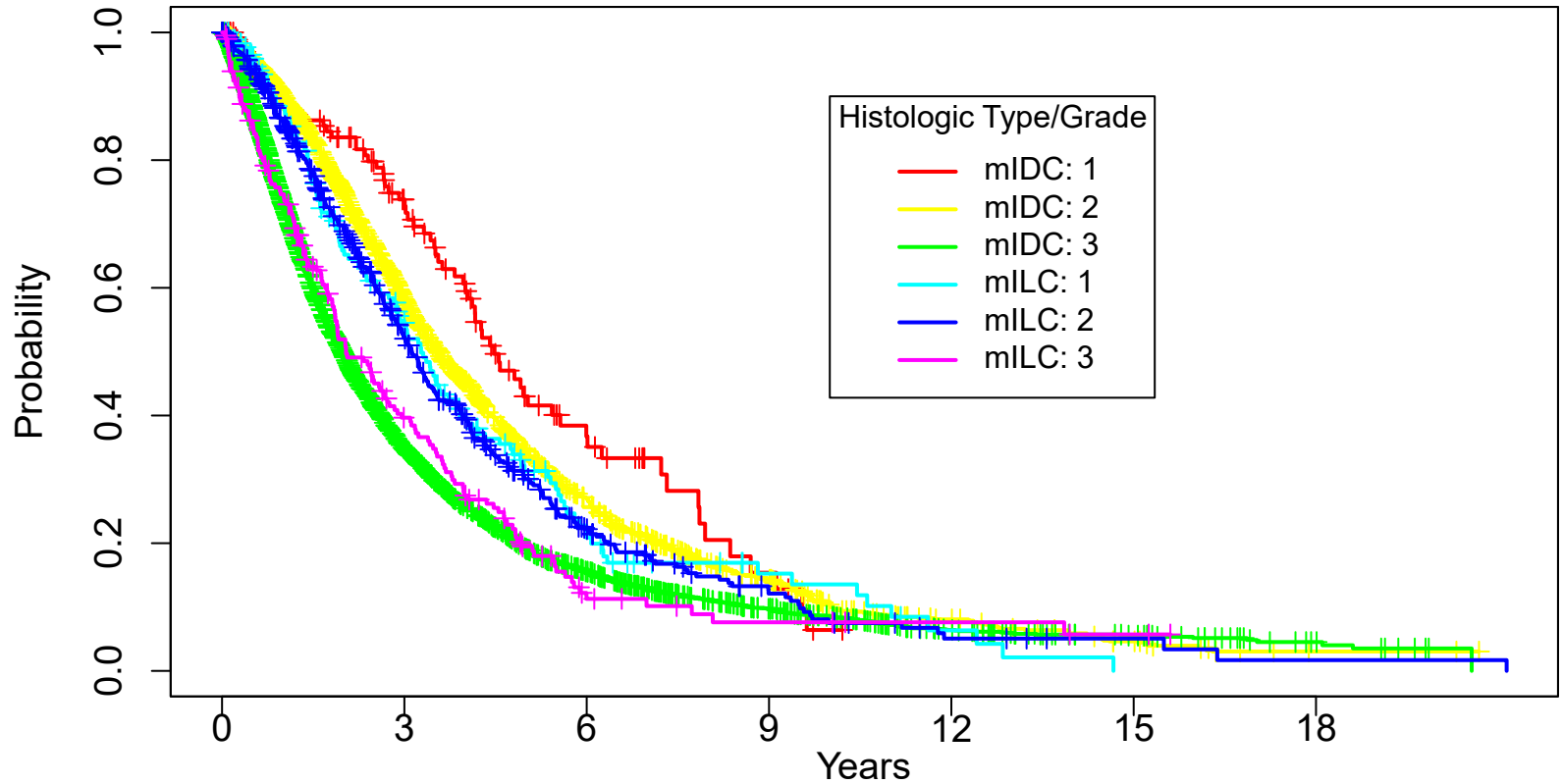
N at risk		0	3	6	9	12	15	18
mIDC: De Novo	—	2407	1084	407	173	60	26	8
mIDC: Recurrent	—	5444	1589	495	174	71	28	5
mILC: De Novo	—	389	191	63	30	11	5	1
mILC: Recurrent	—	700	224	49	15	4		

eFigure 7C: Overall Survival by Histologic Type and ER Percent



N at risk		0	3	6	9	12	15	18
mIDC: 0-9%	—	1868	361	112	52	23	10	2
mIDC: 10-55%	—	695	223	80	28	16	6	1
mIDC: 56-94%	—	1967	805	271	107	32	15	2
mIDC: ≥ 95%	—	2002	884	287	97	31	11	3
mILC: 0-9%	—	70	17	6	3	2		
mILC: 10-55%	—	106	52	9	3	2	1	1
mILC: 56-94%	—	368	143	38	18	5	1	
mILC: ≥ 95%	—	367	128	37	11	3	1	

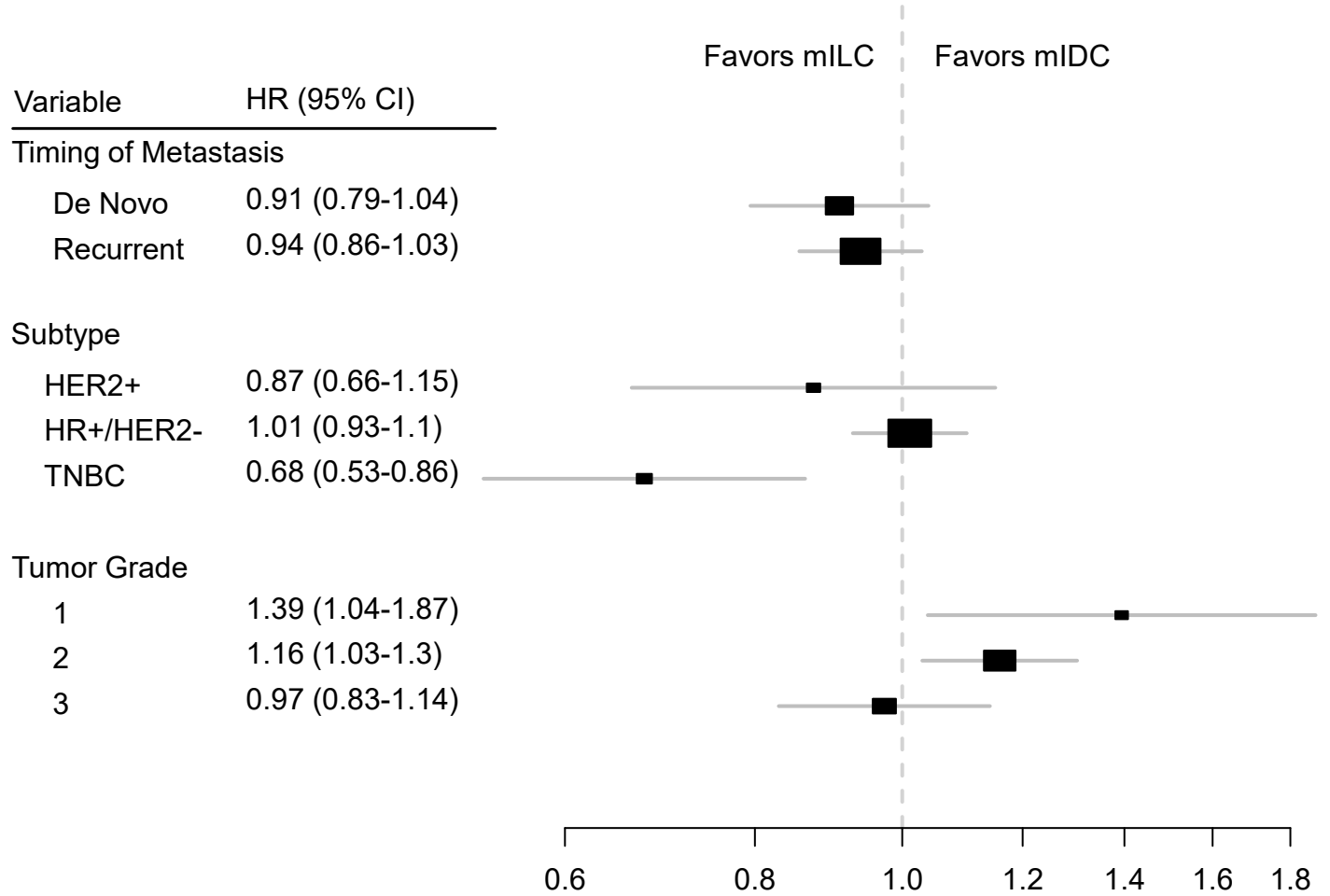
eFigure 7D: Overall Survival by Histologic Type and Tumor Grade



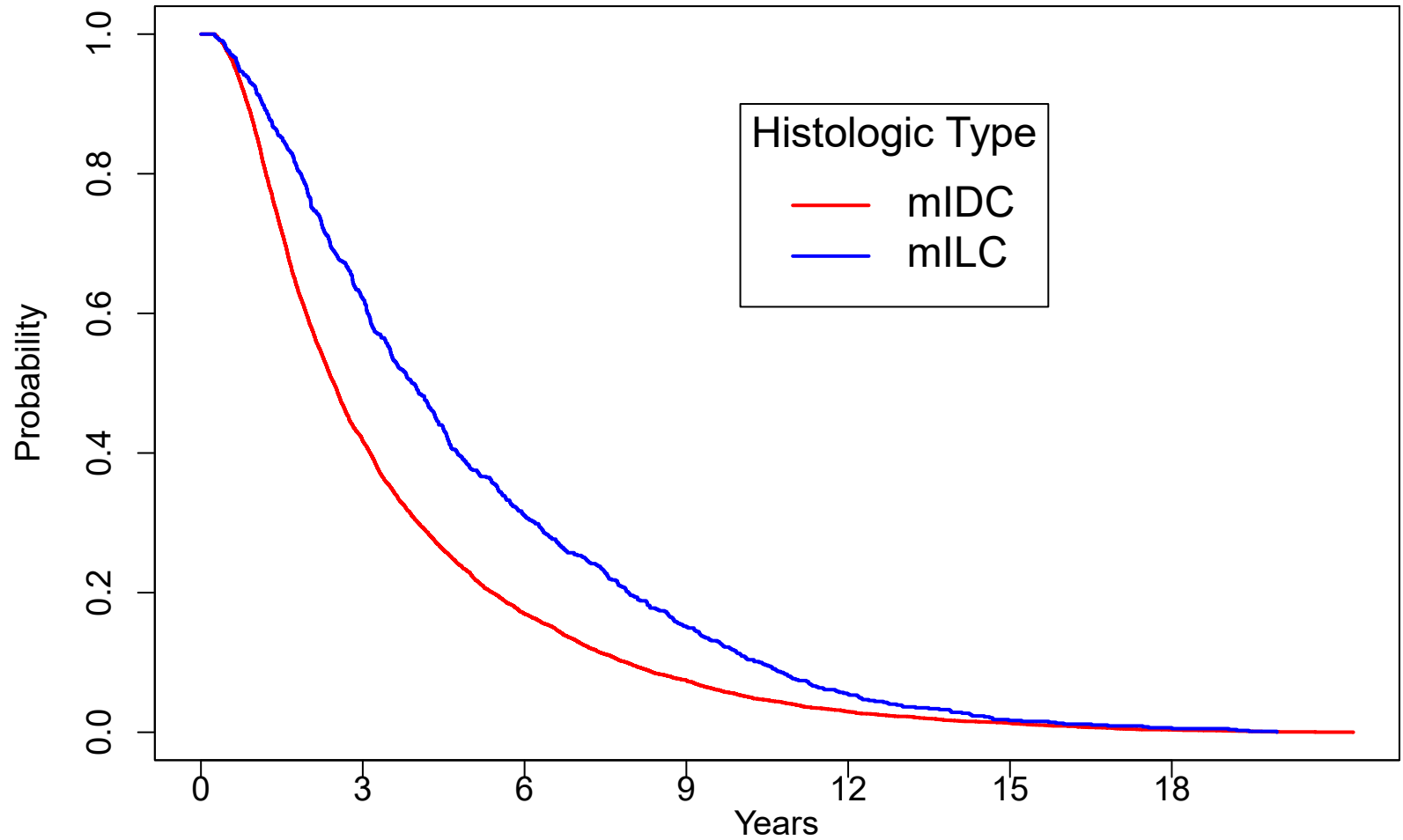
N at risk

mIDC: 1	141	70	22	6			
mIDC: 2	2220	997	343	128	41	16	2
mIDC: 3	4485	1282	442	186	73	34	10
mILC: 1	177	75	22	9	3		
mILC: 2	510	200	59	21	6	3	1
mILC: 3	199	65	12	6	4	2	

eFigure 8: Forest Plot for OS



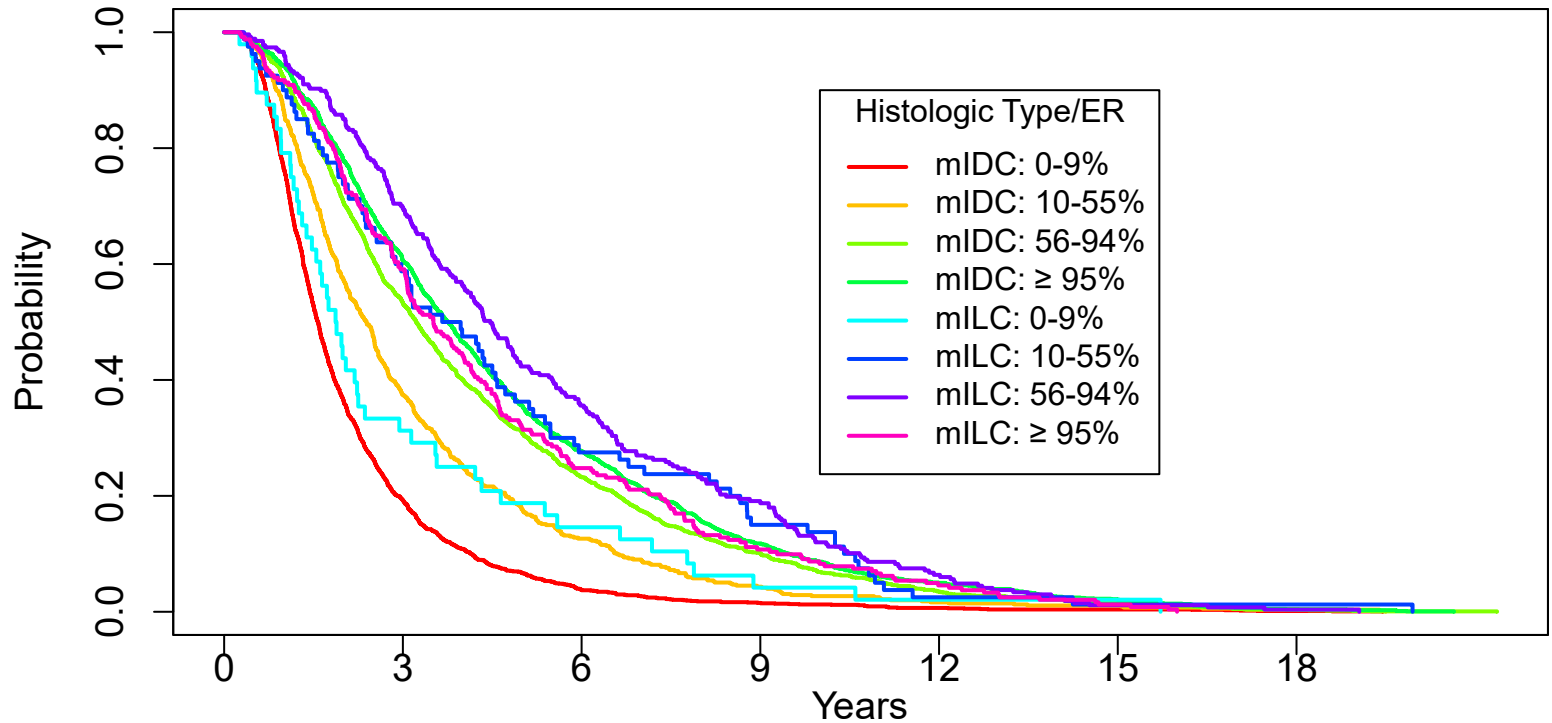
eFigure 9A: Disease-Free Interval by Histologic Type



N at risk

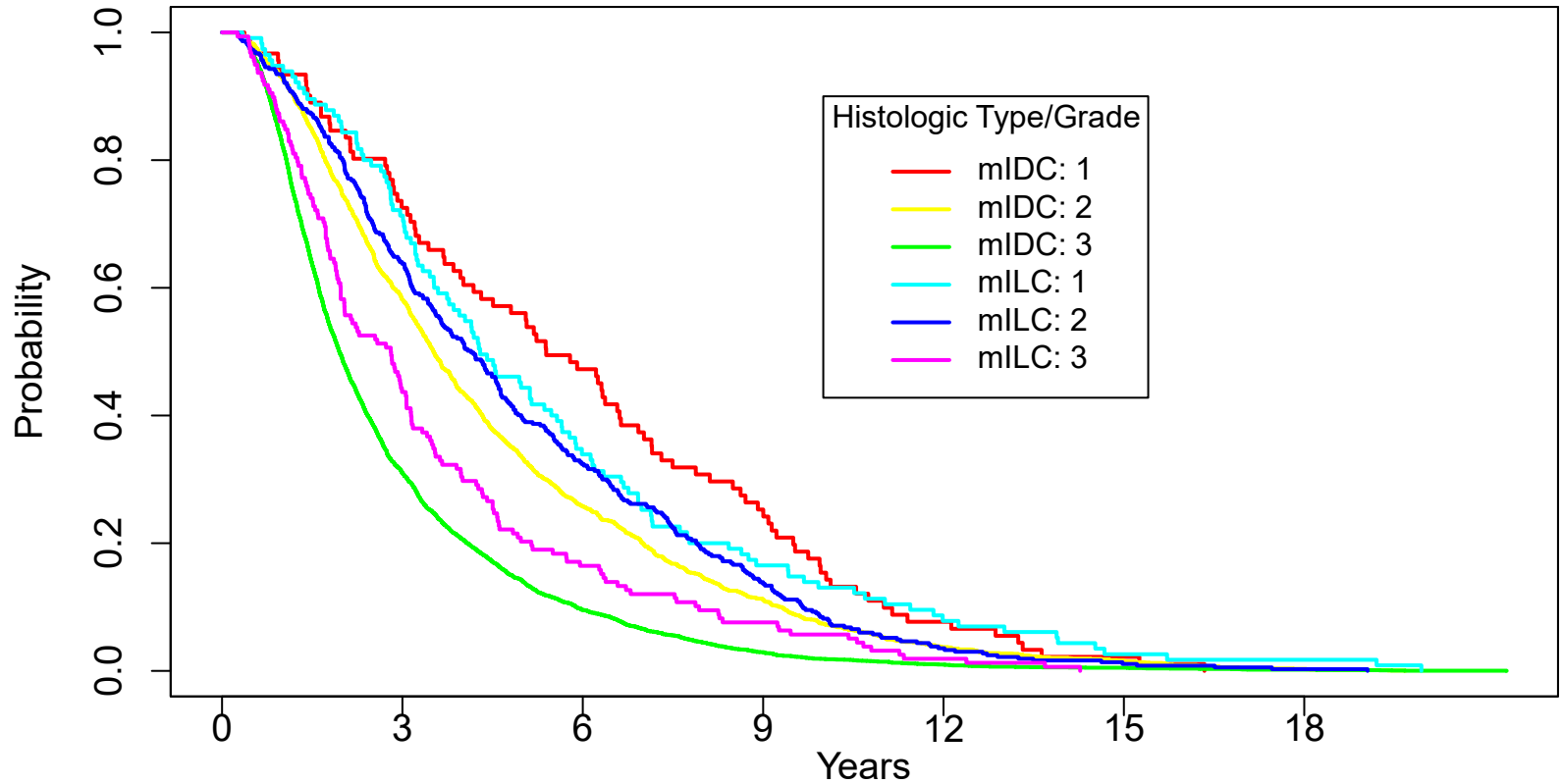
mIDC	6044	2526	1025	451	178	79	21
mILC	770	478	239	116	42	13	5

eFigure 9B: Disease-Free Interval by Histologic Type and Grade



N at risk		0	3	6	9	12	15	18
mIDC: 0-9%	—	1508	291	57	23	10	6	2
mIDC: 10-55%	—	555	208	70	24	9	6	2
mIDC: 56-94%	—	1484	792	345	150	52	23	6
mIDC: ≥ 95%	—	1424	864	394	168	71	30	6
mILC: 0-9%	—	48	15	7	2	1	1	
mILC: 10-55%	—	80	47	22	12	2	1	1
mILC: 56-94%	—	267	186	95	50	17	3	1
mILC: ≥ 95%	—	242	143	60	26	11	3	

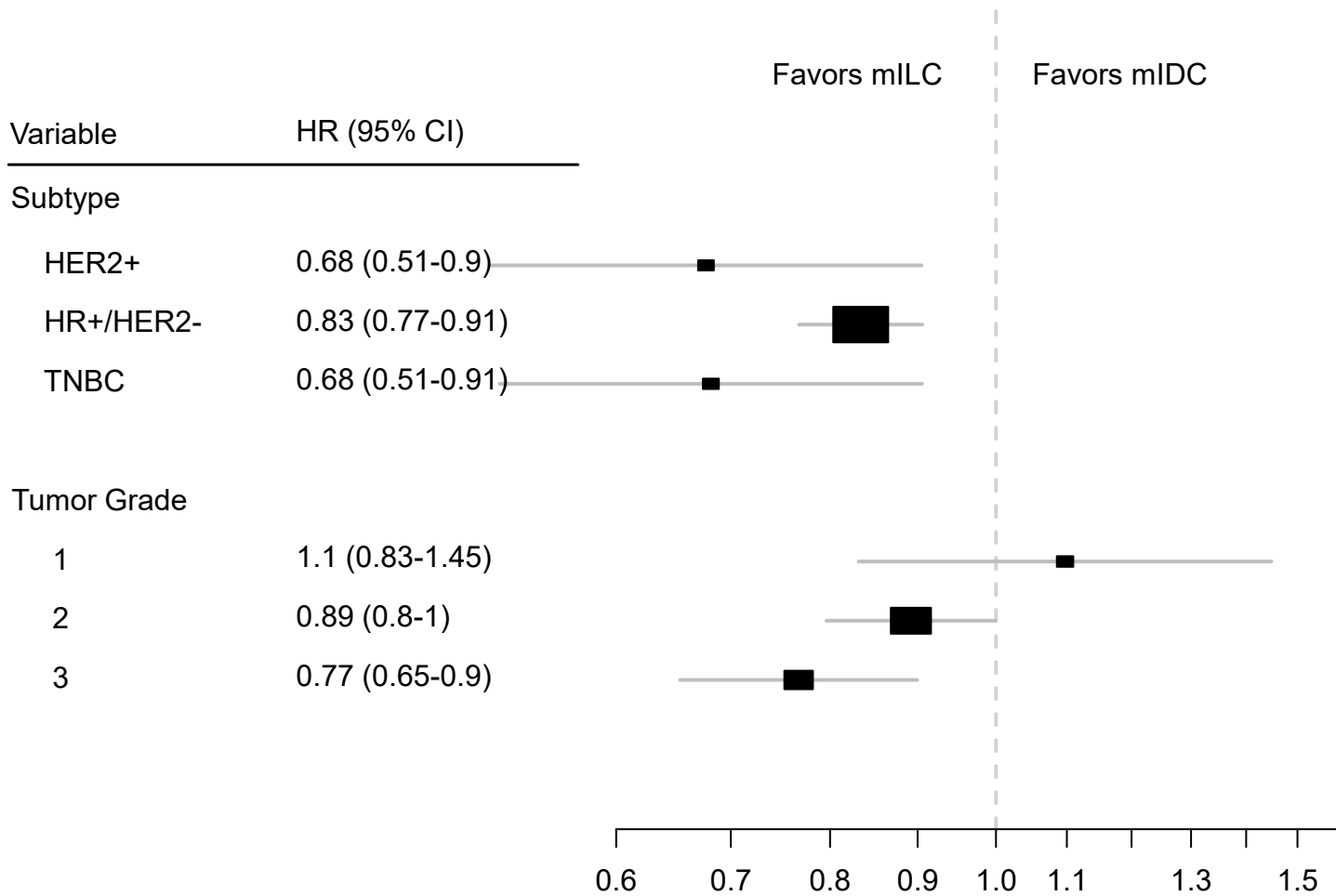
eFigure 9C: Disease-Free Interval by Histologic Type and Tumor Grade



N at risk

mIDC: 1	91	66	43	23	7	2	
mIDC: 2	1609	936	414	180	60	25	5
mIDC: 3	3612	1121	345	106	36	18	7
mILC: 1	115	82	39	19	9	3	2
mILC: 2	367	234	119	50	13	4	1
mILC: 3	158	69	26	12	3		

eFigure 10: Forest Plot for DFI



eFigure 11. Distribution of key genomic alterations according to histologic type across subtypes

