cancers

SUPPLEMENTARY MATERIALS

Table S1. Study characteristics for the included studies.

Indication/Sponsor	Regimen	Comparator	Cohort	ORR (%)	PFS (months)	OS (months)
			IO + IO			
Melanoma (1L) CM-067 BMS [13]	Nivo + Ipi	Ipilimumab	NA	58% vs 19% P<0.00001	11.5 m vs 2.9 m p<0.0001	72.1 m vs 19.9 m p<0.0001
Melanoma (1L) CM-067 BMS [13](	Nivo mono Tx	Ipilimumab	NA	45% vs 19% P<0.00001	6.9 m vs 2.9 m p<0.0001	26.9 m vs 19.9 m p<0.0001
RCC (1L; I/P risk) CM-214 BMS [14]	Nivo + Ipi	Sunitinib	NA	42% vs 27% P<0.001	11.6 m vs 8.4 m p = 0.03 vs (0.009 reqd for signf.)	NR vs 25.9 m p<0.0001
ESCC (1L) (PD-L1 ≥ 1%) CM-648 BMS [15]	Nivo + Ipi	Chemo	NA	35% vs 20%	4.0 m vs 4.4 m , p= 0.90	13.7 m vs 9.1 m p=0.001
Malignant Pleural Mesothelioma (1L) CM-743 BMS [16]	Nivo + Ipi	Chemo	NA	40% vs 43%	6.8 m vs 7.2 m p not reported	18.1 m vs 14.1 m p=0.002
NSCLC (1L) (PD-L1 ≥ 1%) CM-227 BMS [17]	Nivo + Ipi	Chemo	NA	35.9% vs 30%	5.1 m vs 5.6 m p not reported	17.1 m vs 14.9 m p=0.007
			PD – (L)1 Monotherapy			
Melanoma (2L+; post-Ipi) KN-002 – P2 Merck [18]	Pembro mono Tx	Chemo	N=~180 each at 2 DLs	21 – 25 vs 4	2.9 vs 2.7 p<0.001	13.4 vs 11 p=0.117
Melanoma (2L+; post-Ipi) KN-006 – P3 Merck [19]	Pembro mono Tx	Ipi mono Tx	N=~278 at 2 DLs	33 – 34 vs 12	4.1 vs 2.8 p=<0.001	12m OS: 68 vs 58 p=0.0036
Advanced Melanoma CM - 067 BMS [20]	Nivo	Ipi	316 vs 315	45 vs 19	6.9 vs 2.9	36.9 vs 19.9
Melanoma (1L) All-comers CM-067 BMS [13]	Nivo mono Tx	Ipi	316 vs 315	40 vs 14	6.9 vs 2.9 P<0.0001	36.9 vs 19.9 P<0.0001
NSCLC 1L; PD-L1 ≥ 1% KN-042 Merck	Pembro mono Tx	Chemo alone	637 vs 637	27.3 vs 26.5	5.4 vs 6.5	16.7 vs 12.1 P=0.0036

[21]						
NSCLC (IO-naïve; post-chemo PD-L1 ≥ 1%) KN-010 Merck [22]	Pembro mono Tx	docetaxel	346 vs 343	21.2 vs 9.6 P<0.001	4.0 vs 4.1 P=0.005	11.8 vs 8.4 P<0.001
HNSCC (1L) PD-L1 ≥ 1%) KN-048 Merck [23]	Pembro mono Tx	Cetuximab + platinum chemo + FU	257 vs 255	19 vs 35	3.2 vs 5.0	12.3 vs 10.3 P=0.0171
Urothelial 2L+; post-plt chemo KN-045 Merck [24]	Pembro mono Tx	Chemo	270 vs 272	21.1 vs 11.4	2.1 vs 3.3 P=0.833	10.3 vs 7.4 P=0.004
mESCC 2L+; PD-L1 ≥ 10 KN-181 Merck [25]	Pembro mono Tx	Chemo	85 vs 82	22 vs 7	3.2 vs 2.3	10.3 vs 6.7 P=0.0074
HCC (2L+) post-sorafenib/ chemo KN-394 Merck [26]	Pembro mono Tx	Placebo	222 vs 128	13.7 vs 1.3 P<0.0001	2.6 vs 2.3 P=0.0032	13.9 vs 10 -=0.180
Gastric/GEJ 2L+ (post-plt-chemo) PD-L1 ≥ 1% KN-061 Merck [27]	Pembro mono Tx	Paclitaxel	196 vs 199	16 vs 14	1.5 vs 4.1 m p=0.98	9.1 vs 8.3 m p=0.042
Gastric/GEJ 1L PD-L1 ≥ 1 or 10 KN-062 Merck [28]	Pembro mono Tx	Chemo alone	256 vs 250	15 vs 37	2.0 vs 6.4	10.6 vs 11.1
CRC 1L MSI-H KN-177 Merck [29]	Pembro mono Tx	Chemo alone	153 vs 154	43.8 vs 33.1	16.5 vs 8.2 p=0.0004	NR vs 36.7 p=0.0359
NPC 2L+ All-comers KN-122 Merck [30]	Pembro mono Tx	Chemo alone	117 vs 116	21.4 vs 23.5	4.1 vs 5.5	17.2 vs 15.2 p=02262
HCC 3L+ All-comers KN-240 Merck [31]	Pembro mono Tx	BSC	278 vs 135	18.3 vs 4.4	3 vs 2.8m p=0.0209	13.9 vs 10.6 p=0.0238
Bladder 1L All-comers KN-361 Merck	Pembro mono Tx	Chemo alone	307 vs 352	30 vs 45	3.9 vs 7.1 m p=untested	15.6 vs 14.3 p=untested

[32]						
Gastric/GEJ KN-063 Merck [33]	Pembro mono Tx	Chemo alone	47 vs 47	12.8 vs 19.1	1.9 vs 4.0 m	8.4 vs 7.7 m
PD – (L)1 + Chemotherapy						
Urothelial (1L) IMvigor130 Roche [34]	Atezo + chemo	Chemo alone	447 vs 397	48.1 vs 44.8	8.2 vs 6.3 P=0.007	16.1 vs 13.4 p=0.023 (NS)
Urothelial (1L) KN-361 Merck [35]	Pembro + chemo	Chemo alone	351 vs 352	55 vs 45	8.3 vs 7.1 P=0.0033	17 vs 14.3 P=0.0407
BTC KN-966 Merck [36]	Pembro + chemo	Placebo + Chemo	533 vs 536	29 vs 29	6.5 vs 5.6 P = NS	12.7 vs 10.9 P=0.0034
Endometrial (1L dMMR) KN-868 Merck [37]	Pembro + chemo	Chemo alone	112 vs 113	81.5 vs 70.7 OR: 1.83	NR vs 7.6 P<0.00001	NR vs NR p-=0.0617
Endometrial (1L pMMR) KN-868 Merck [37])	Pembro + chemo	Chemo alone	293 vs 295	70.7 vs 58.1 OR: 1.74	13.1 vs 8.7 P<0.001	NR vs 27.37 P=0.1157
HNSCC (R/M) KN-048 Merck [23]	Pembro + chemo	Cetuximab (EGFRi) + chemo	281 vs 278	36 vs 36	4.9 vs 5.1 p=0.1697	13.0 vs 10.7 p=0.0034
Multiple Myeloma 1L All-comers KN-185 Merck [38]	Pembro + chemo	Chemo alone	149 vs 145	64 vs 62	NR vs NR p=0.75	NR vs NR P=0.97
Gastric/GEJ 1L PD-L1 ≥ 1 or 10 KN-062 Merck [28]	Pembro + chemo	Chemo alone	257 vs 250	49 vs 37	2.0 vs 6.4	12.5 vs 11.1 p=0.05
Multiple Myeloma KN-183 Merck [39]	Pembro + chemo	Chemo alone	125 vs 124	34 vs 40	5.7 vs 7.4 m p=0.98	NR vs 15.2 p=0.95
Non-Sq NSCLC KN-189 Merck [40]	Pembro + chemo	Platinum based chemo	405 vs 202	47.6 vs 18.9	8.8 vs 4.9 p<0.001	NR vs 11.3 p<0.001
Sq. NSCLC 1L All-comers KN-407 Merck [41]	Pembro + chemo	Platinum based chemo	278 vs 281	57.9 vs 28.4	6.4 vs 4.8 m p<0.0001	15.9 vs 11.3 p=0.0017
TNBC 1L PDL1 ≥ 10 KN-355 Merck	Pembro + chemo	Chemo alone	220 vs 103	52.7 vs 40.8	9.7 vs5.6 m p=0.0012	23 vs 16.1 p=0.0093

[42]						
Esophageal 1L All-comers KN-590 Merck [43]	Pembro + chemo	Platinum based chemo	373 vs 376	45 vs 29.3	6.3 vs 5.8 m p<0.0001	12.4 vs 9.8 p=0.001
PD – (L)1 + CTL4-A						
Urothelial (1L) DANUBE Astrazeneca [32]	Durva + treme	Chemo	342 vs 344	36 vs 49	3.7 vs 6.7	15.1 vs 12.1 p=0.075
Advanced Melanoma CM – 067 BMS [20]	Nivo + Ipi	Ipi	314 vs 315	58 vs 19	11.5 vs 2.9	60 vs 19.9
Melanoma (1L) BRAFV600E Wt CM-069 BMS [43]	Nivo + Ipi	Ipi alone	72 vs 37	60 vs 11 P<0.001	8.9 vs 4.7 P<0.002	NR vs 24.8 p=0.09
Melanoma (1L) All-comers CM-067 BMS [13]	Nivo + Ipi	Ipi	314 vs 315	58 vs 19	11.5 vs 2.9 P<0.0001	72.1 vs 19.9 P<0.0001
NSCLC 1L PD-L1 ≥ 50% KN-598 Merck [44]	Pembro + Ipi	Pembro monoTx	284 vs 284	45.4 vs 45.4	8.2 vs 8.4m ; p=0.72	21.4 vs 21.9 p=0.74
NSCLC PD-L1 >1% CM-227 BMS [17]	Nivo + Ipi	Platinum based chemo	582 vs 583	35.9 vs 30.0	5.1 vs 5.6 m p: Not rep	17.1 vs 14.9 p=0.007
Malignant Pleural Mesothelioma CM-743 BMS [16]	Nivo + Ipi	Chemo	303 vs 302	40 vs 43	6.8 vs 7.2	18.1 vs 14.1 p=0.002
NSCLC 1L All-comers CM-9LA BMS [45]	Nivo + Ipi + chemo	Chemo alone	361 vs 358	38.2 vs 24.9	6.8 vs 5.0 P=0.00012	14.1 vs 10.7 p=0.0006
PD – (L)1 + TKI						
Endometrial 2L+ KN-775 Merck [46]	Pembro + Lenvatinib	Doxorubicin or Paclitaxel	346 vs 351	30 vs 15	6.6 vs 3.8	17.4 vs 12 P=0.0001
RCC KN-426 Merck [47]	Pembro + axitinib	Sunitinib	432 vs 429	60.4 vs 39.6	15.7 vs 11 p<0.0001	45.7 vs 40 p=0.001
RCC KN-581 Eisai	Pembro + lenvatinib	Sunitinib	355 vs 357	71.0 vs 36.1	23.9 vs 9.2 p<0.001	NR vs NR P=0.005

[14]						
HCC LEAP-002 Merck [48]	Pembro + Lenvatinib	Lenvatinib	395 vs 399	27.8 vs 16.8	8.2 vs 8.0 m p=0.0466	21.2 vs 19 p=0.0227
Melanoma LEAP-003 Merck [49]	Pembro + Lenvatinib	Pembro monoTx	334 vs 340	40.4 vs 34.1	10.1 vs 4.2	25.8 vs 39.5
NSCLC 1L All-comers; Non-Sq LEAP-006 Merck [22]	Pembro + lenvatinib + Plt- chemo	Pembro + plt-chemo	375 vs 373	60.0 vs 53.6	12.2 vs 9.2	21.8 vs 22.1 P=0.708
Bladder cancer LEAP-011 Merck [50]	Pembro + Lenvatinib	Pembro alone	245 vs 242	33.1 vs 28.9	4.5 vs 4.0 m	11.8 vs 12.9
NSCLC LEAP-008 Merck [51]	Pembro + Lenvatinib	Docetaxel	185 vs 189	22.7 vs 14.3	5.6 vs 4.2	11.3 vs 12.0 P=0.4342
HNSCC LEAP-10 Merck [52]	Pembro + Lenvatinib	Pembro + placebo	256 vs255	46.1 vs 25.4	6.2 vs 2.8 P=0.0001	15.0 vs 17.9 P=0.882
MSS-CRC LEAP-017 Merck [53]	Pembro + Lenvatinib	Rego/ TAS-102	241 vs 239	10.4 vs 1.7	3.8 vs 3.3	9.8 vs 9.3 m p=0.0379

Table S2. Summary Statistics for ORR, PFS and OS.

Mean ORR		**Mean PFS**		**Mean OS**	
Experimental	**Comparator**	**Experimental**	Comparator	Experimental	Comparator
IO + IO					
42.18%	27.8%	7.8 months	5.7 months	30.25 months	16.78 months
PD – L (1) Monotherapy					
21.48%	17.38%	3.12 months	4.24 months	12.26 months	9.64 months
PD – L (1) + Chemotherapy					
48.24%	32.42%	7.94 months	5.6 months	17.9 months	12.58 months
PD – L (1) + CTLA-4					
50%	23%	11.55 months	5.65 months	72.1 months	22.9 months
PD – L (1) + TKI					
53.06%	30.83%	15.93 months	9.4 months	33.45 months	29.67 months
Cumulative Results					
42.5%	26.1%	8.55 months	5.53 months	26.77 months	17.18 months

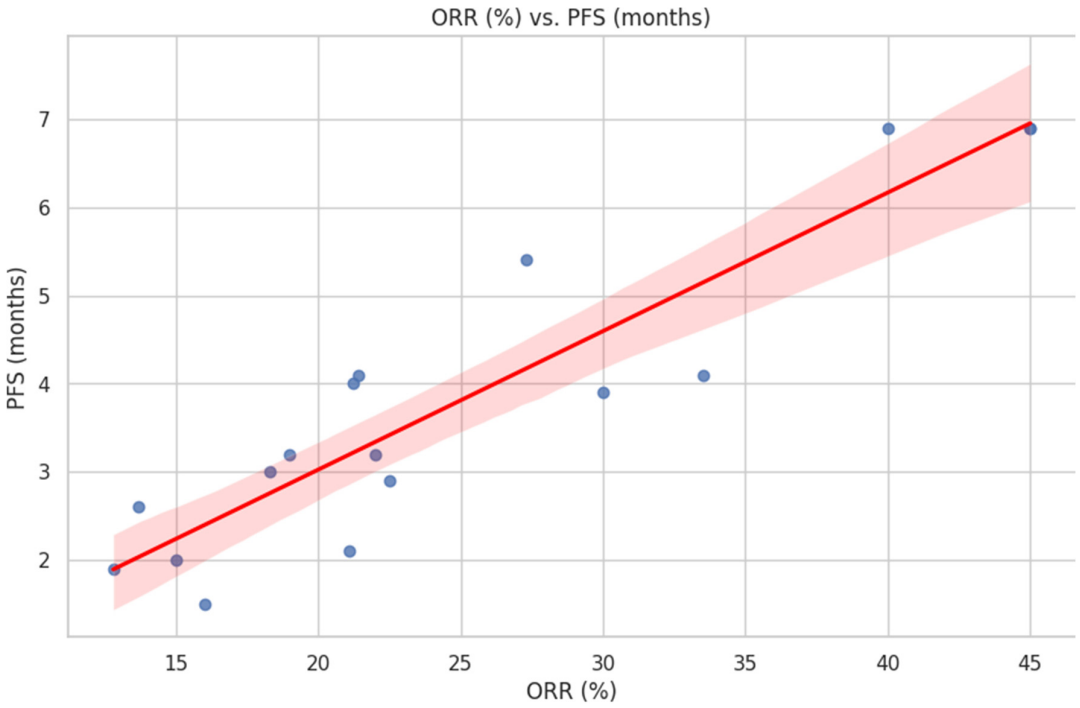


Figure S1. Correlation Between ORR and PFS in Patients Undergoing PD-(L)1 Therapy.

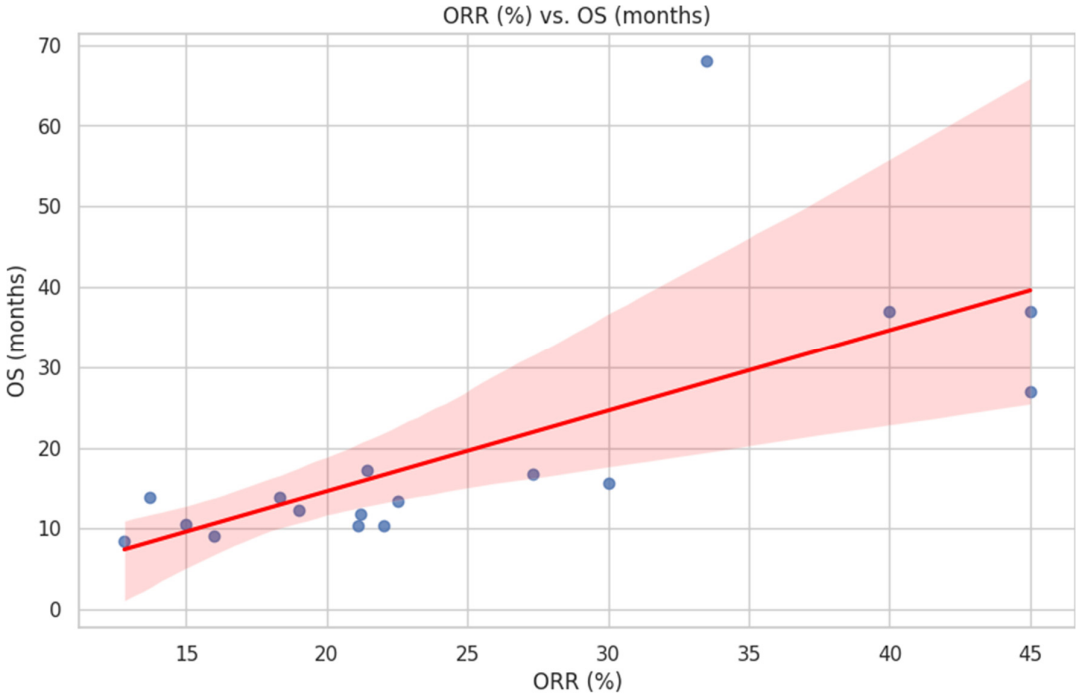


Figure S2. Correlation Between ORR and OS in Patients Undergoing PD-(L)1 Therapy.

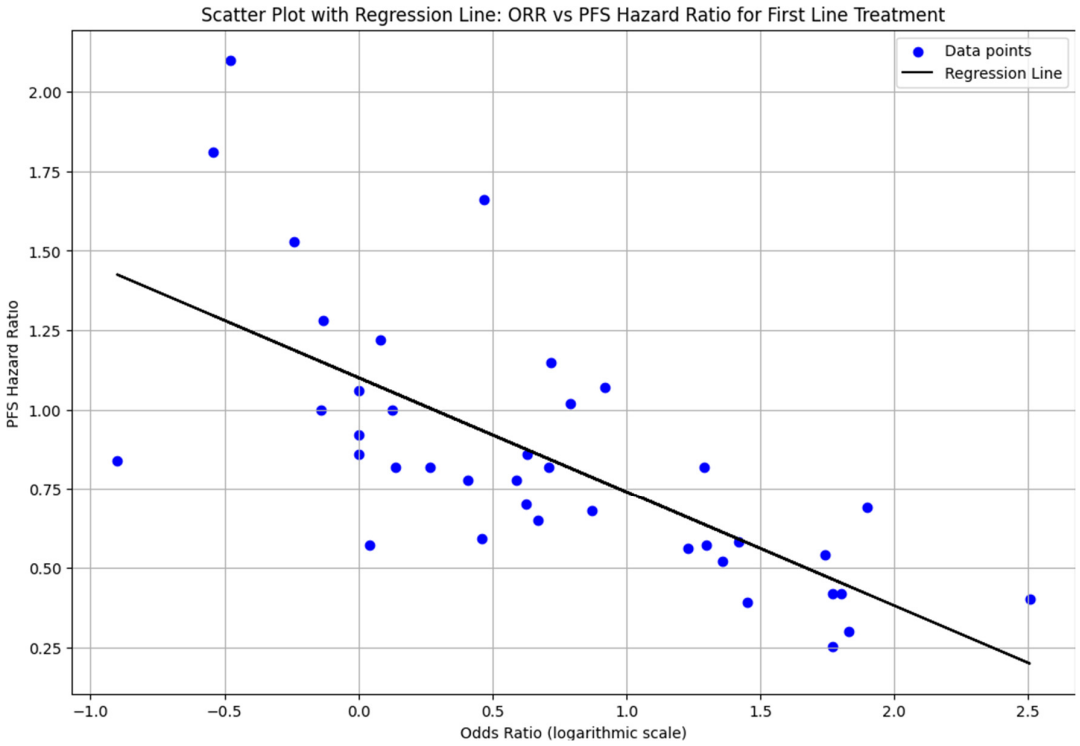


Figure S3. First Line Treatment (PFS).

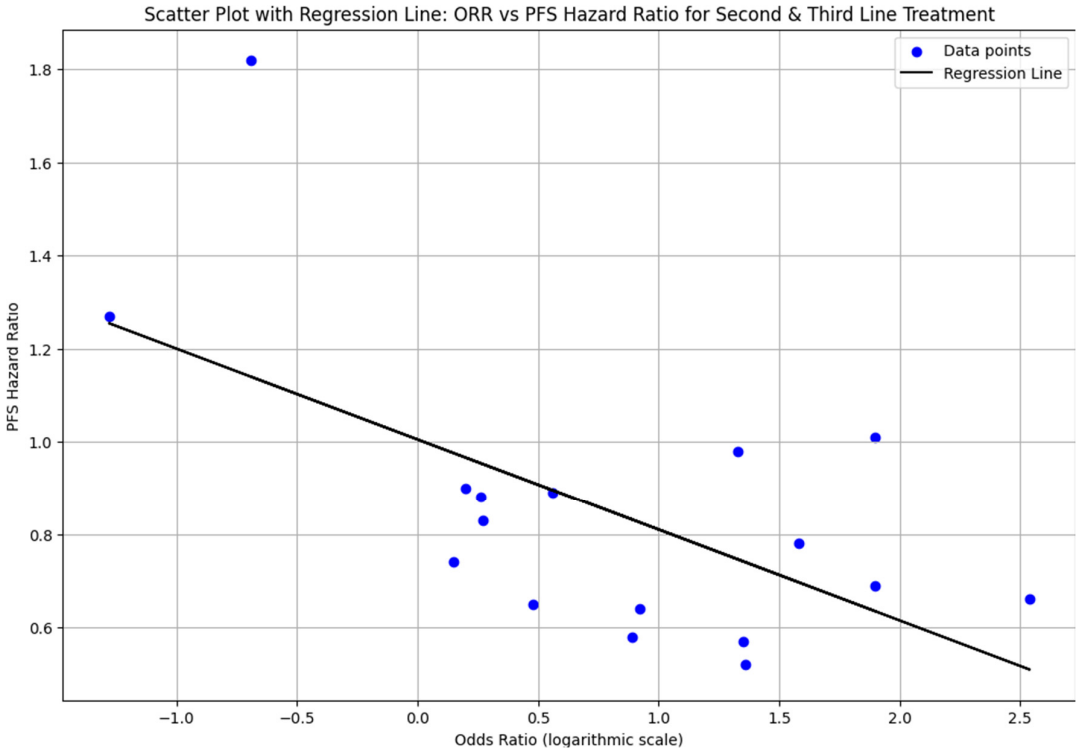


Figure S4. Second & Third Line Treatment (PFS).

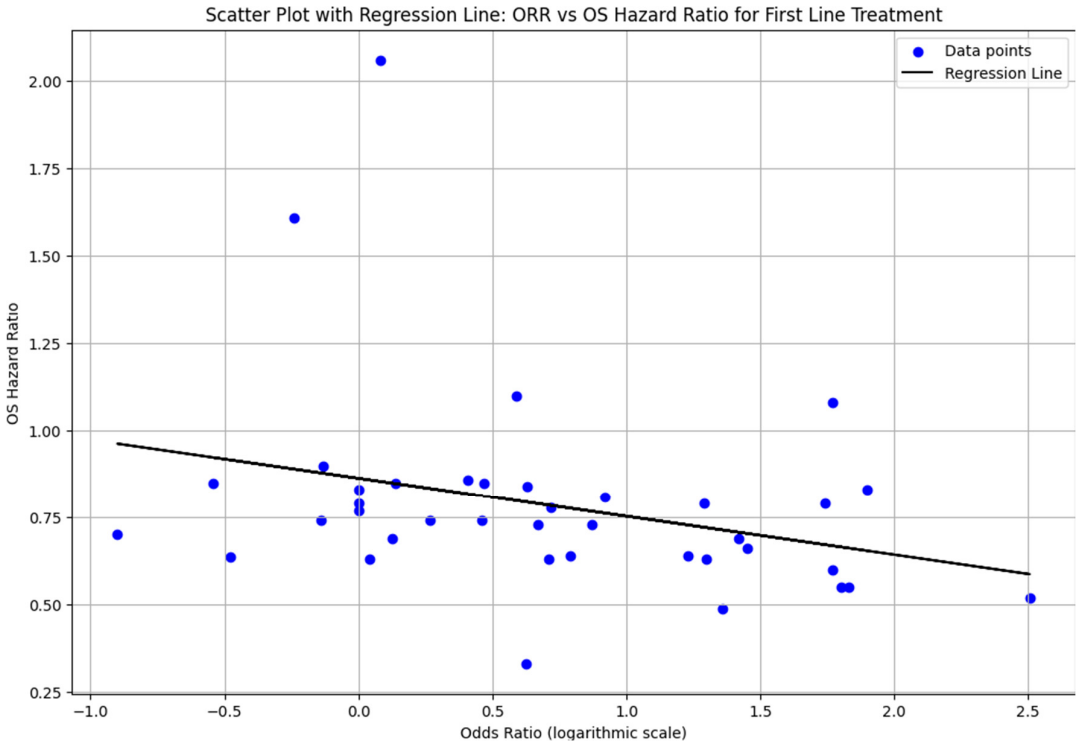


Figure S5. First Line Treatment (OS).

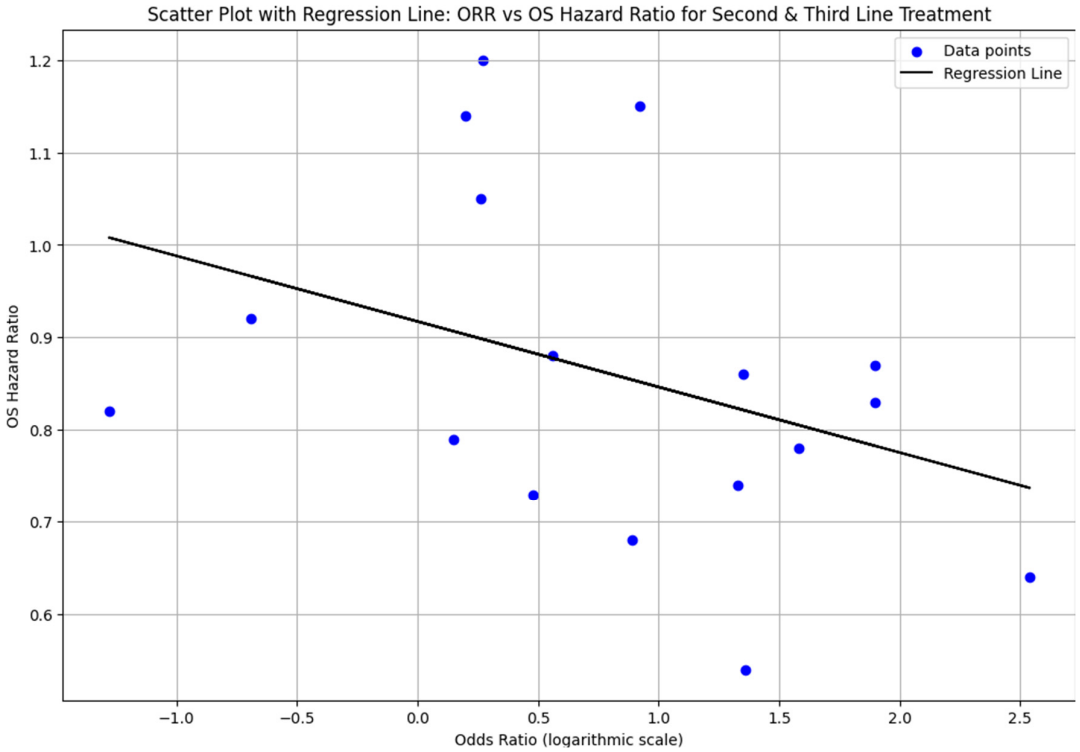


Figure S6. Second and Third Line Treatment (OS).