SUPPLEMENTARY FIGURES

Variable	N	Hazard ratio		P
Age				
> 60	808	■	Reference	
≤ 60	555	⊢■⊣	1.08 (0.92, 1.27)	0.326
Gender				
Female	496	■	Reference	
Male	867	⊢■⊣	0.93 (0.79, 1.10)	0.401
Cancer subtype				
BG	115	■	Reference	
BLCA	211	⊢■⊣	0.78 (0.57, 1.07)	0.123
CRC	109	⊢■⊣	0.75 (0.51, 1.09)	0.132
HNSC	129	⊢■⊣	1.02 (0.74, 1.40)	0.908
NSCLC	344	⊢■⊣	0.98 (0.74, 1.28)	0.865
RCC	142	⊢■⊣	0.32 (0.22, 0.45)	<0.001
SKCM	313	⊢■⊣	0.49 (0.35, 0.69)	<0.001
Drug target				
Combination	204	■	Reference	
CTLA-4	76	⊢■⊣	1.13 (0.73, 1.73)	0.582
PD−1/PD-L1	1083	⊢■⊣	1.66 (1.27, 2.16)	<0.001
TMB				
High	682	■	Reference	
Low	681	⊢■⊣	1.12 (0.95, 1.33)	0.118
MSH2				
Wild type	1328	■	Reference	
Mutated	35	⊢■⊣	0.62 (0.33, 1.17)	0.149
MRE11A				
Wild type	1339	■	Reference	
Mutated	24	⊢■⊣	0.42 (0.17, 1.01)	0.039
NBN				
Wild type	1337	■	Reference	
Mutated	26	⊢■⊣	0.66 (0.31, 1.42)	0.292
BRCA2				
Wild type	1280	■	Reference	
Mutated	83	⊢■⊣	0.89 (0.62, 1.28)	0.535
RAD51C				
Wild type	1352	■	Reference	
Mutated	11	⊢■⊣	0.67 (0.21, 2.15)	0.511
ATM				
Wild type	1274	■	Reference	
Mutated	89	⊢■⊣	0.70 (0.49, 1.02)	0.046
POLE				
Wild type	1289	■	Reference	
Mutated	74	⊢■⊣	0.73 (0.48, 1.09)	0.122
PARP1				
Wild type	1342	■	Reference	
Mutated	21	⊢■⊣	0.57 (0.21, 1.57)	0.281

0.2   0.5   1   2

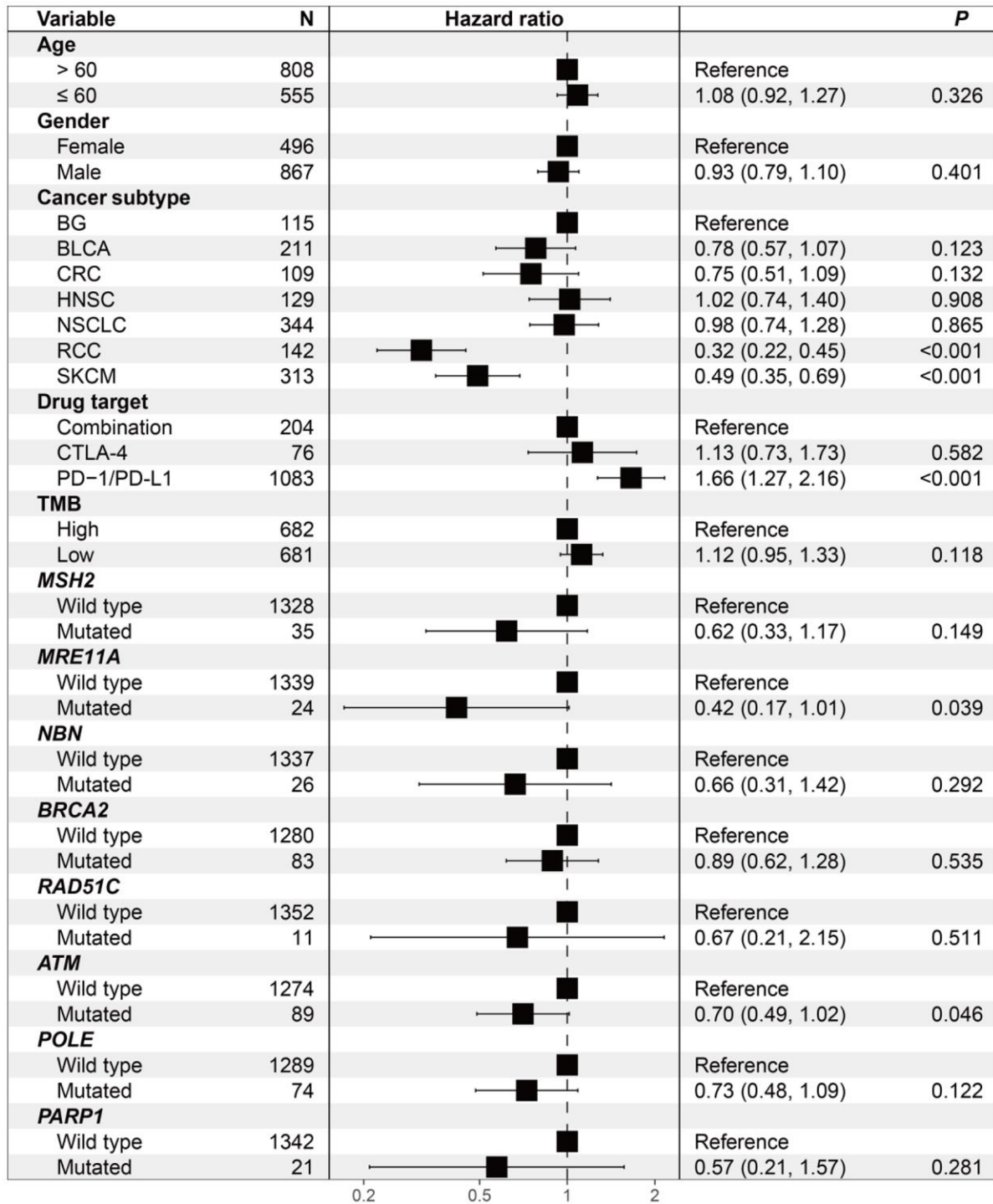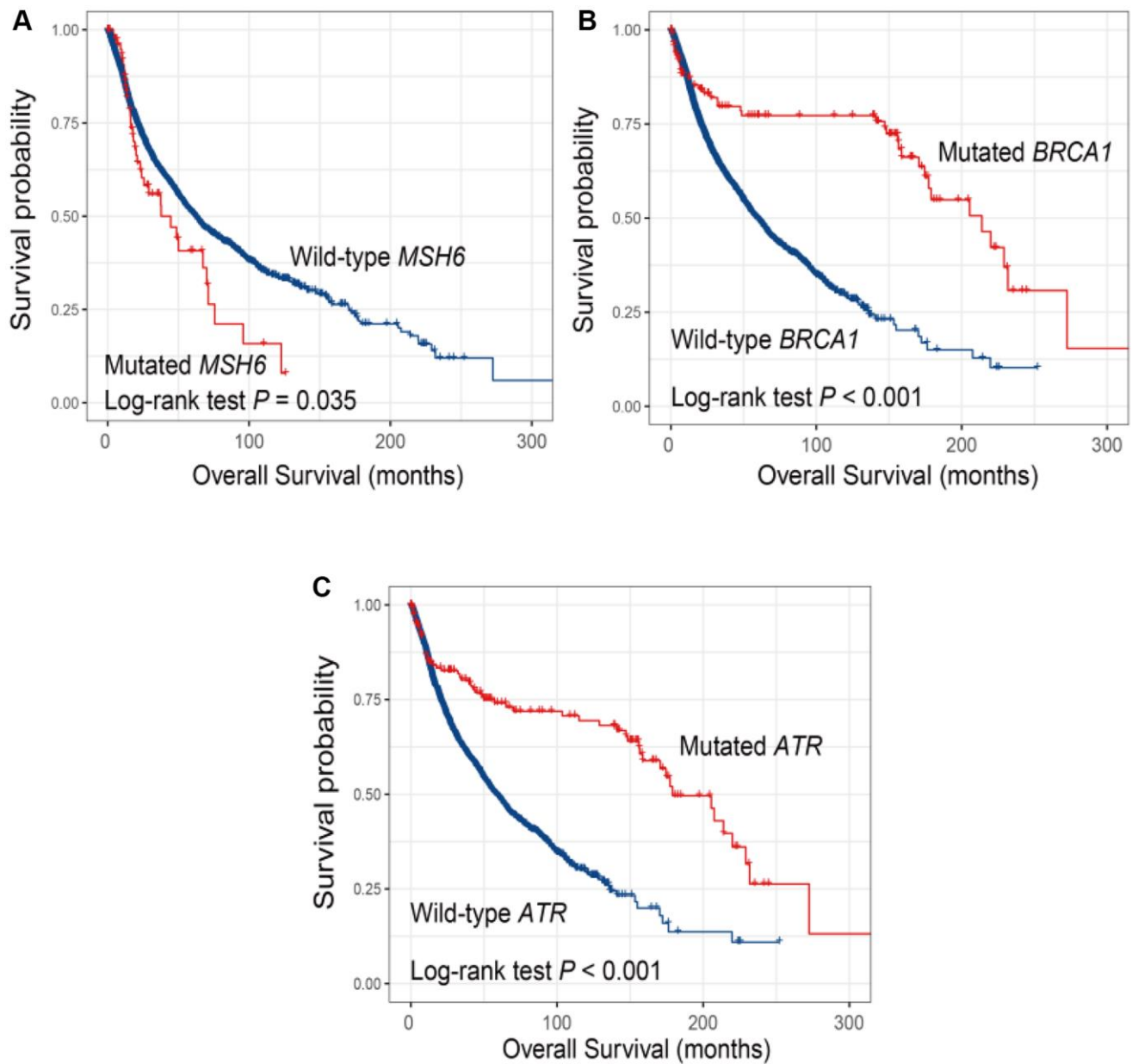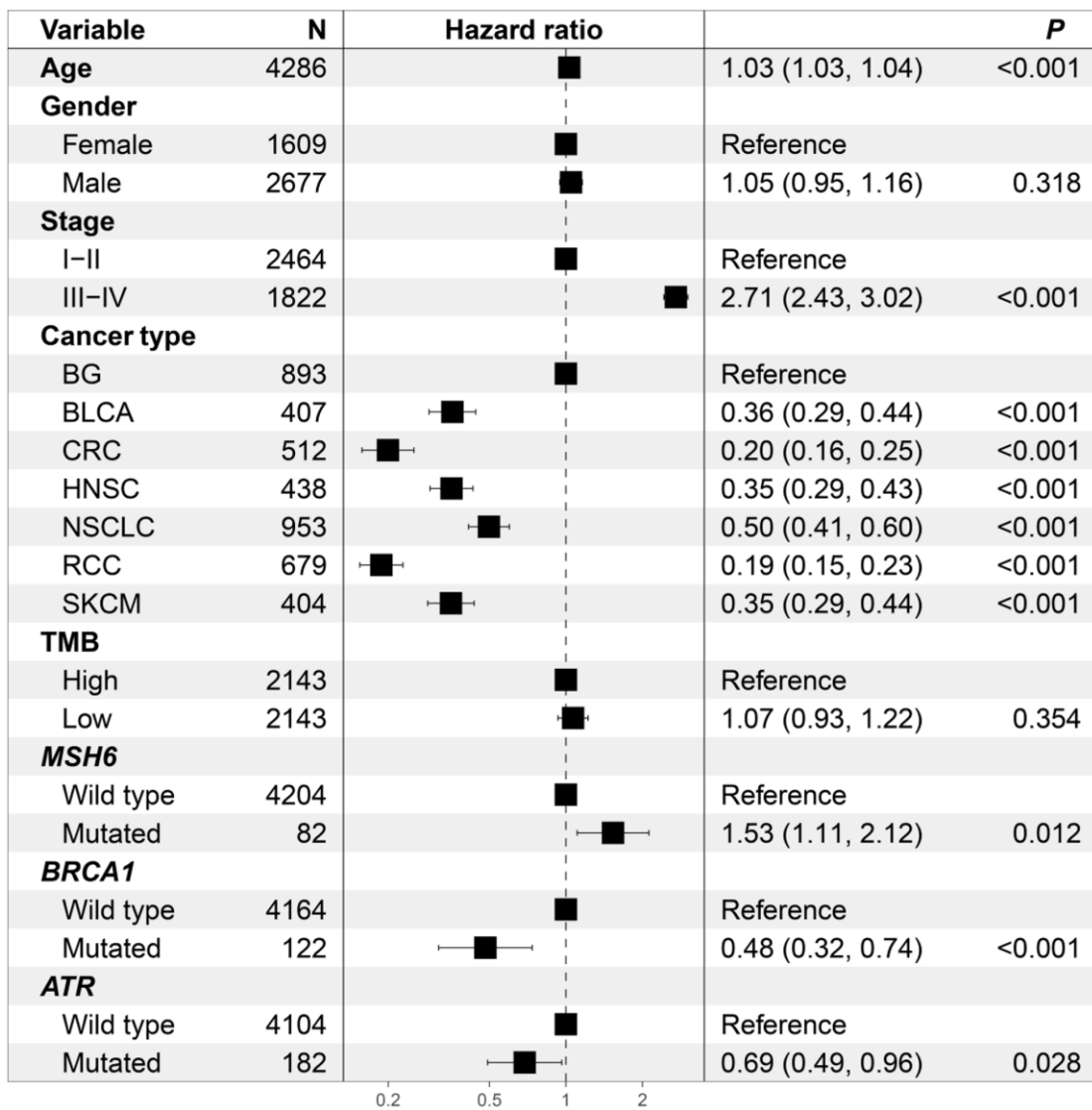**Supplementary Figure 1. Multivariate Cox regression model was conducted with clinical confounding factors and identified 8 DDR genes mutations taken into consideration in the MSKCC cohort.**

Supplementary Figure 2. Kaplan-Meier survival curves of mutations in 3 DDR genes in the TCGA cohort. Survival curves representation of mutations in (**A**) *MSH6*, (**B**) *BRCA1*, and (**C**) *ATR*.

Variable	N	Hazard ratio		P
Age	4286	■	1.03 (1.03, 1.04)	<0.001
Gender				
Female	1609	■	Reference	
Male	2677	■	1.05 (0.95, 1.16)	0.318
Stage				
I−II	2464	■	Reference	
III−IV	1822	■	2.71 (2.43, 3.02)	<0.001
Cancer type				
BG	893	■	Reference	
BLCA	407	├■┤	0.36 (0.29, 0.44)	<0.001
CRC	512	├■┤	0.20 (0.16, 0.25)	<0.001
HNSC	438	├■┤	0.35 (0.29, 0.43)	<0.001
NSCLC	953	├■┤	0.50 (0.41, 0.60)	<0.001
RCC	679	├■┤	0.19 (0.15, 0.23)	<0.001
SKCM	404	├■┤	0.35 (0.29, 0.44)	<0.001
TMB				
High	2143	■	Reference	
Low	2143	├■	1.07 (0.93, 1.22)	0.354
MSH6				
Wild type	4204	■	Reference	
Mutated	82	├■┤	1.53 (1.11, 2.12)	0.012
BRCA1				
Wild type	4164	■	Reference	
Mutated	122	├■┤	0.48 (0.32, 0.74)	<0.001
ATR				
Wild type	4104	■	Reference	
Mutated	182	├■┤	0.69 (0.49, 0.96)	0.028

0.2   0.5   1   2

Supplementary Figure 3. Multivariate Cox regression model was conducted with clinical confounding factors and identified 3 DDR genes mutations taken into consideration in the TCGA cohort.