

Figure S1. Expression of ESCC cancer stemness-associated DNA damage repair genes. (A) Expression of PARP4, DDX11, and RAD17 in high and low cancer stemness of ESCC. (B) Expression of PARP4 in various human cancers. T, tumor tissues; N, normal tissues; PARP4, poly(ADP-ribose) polymerase family member 4; ESCC, esophageal squamous cell carcinoma; DDX11, DEAD/H-Box Helicase 11; RAD17, RAD17 checkpoint clamp loader component; SI, stemness index.

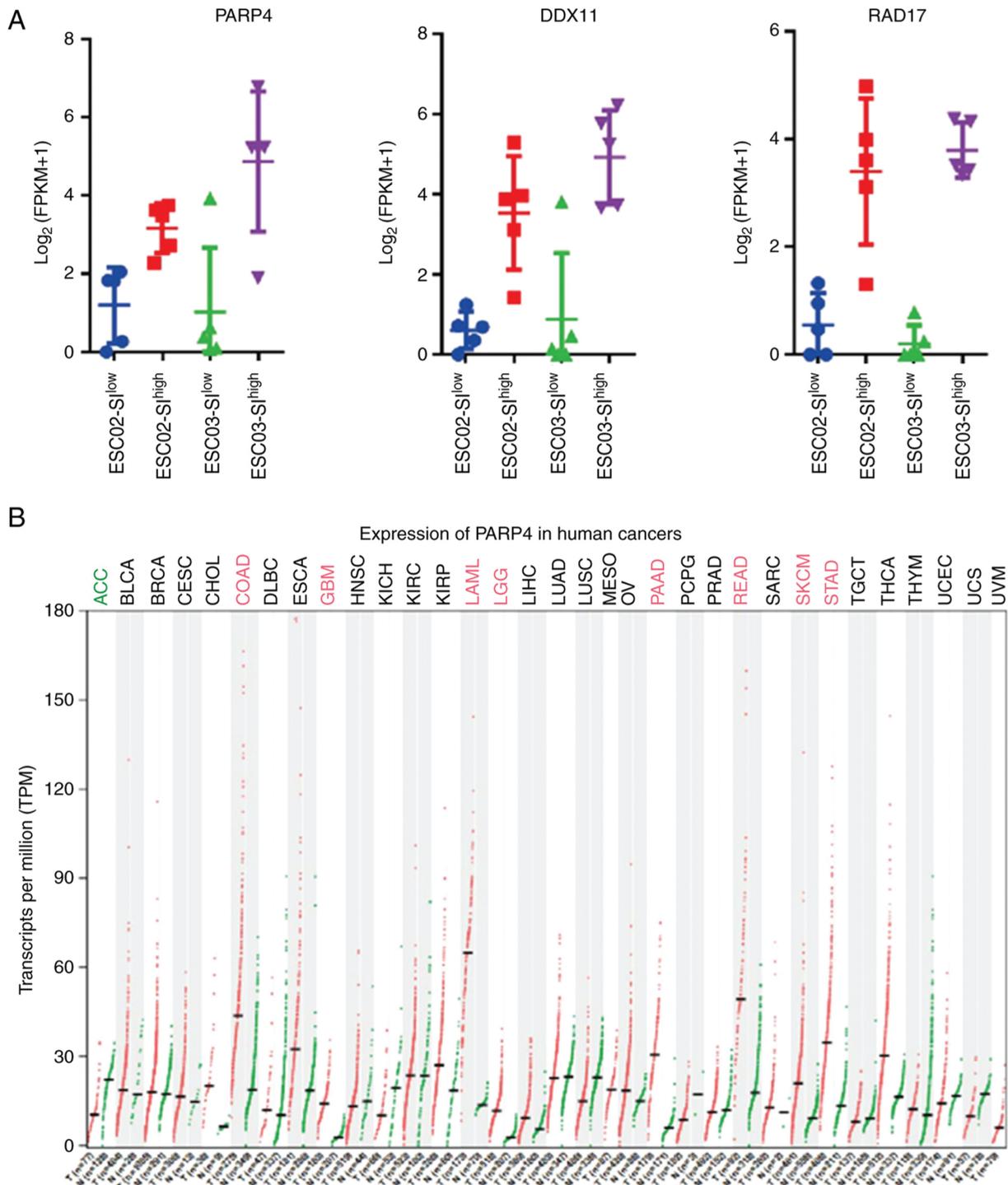


Figure S2. Upregulated PARP4 correlates with shorter overall survival and disease-free survival in CESC and LUSC, but not EAC. TPM, Transcripts per Kilobase Million; HR, hazard ratio; n, patient number; PARP4, poly(ADP-ribose) polymerase family member 4; CESC, cervical squamous cell carcinoma; LUSC, lung squamous cell carcinoma; EAC, esophageal adenocarcinoma.

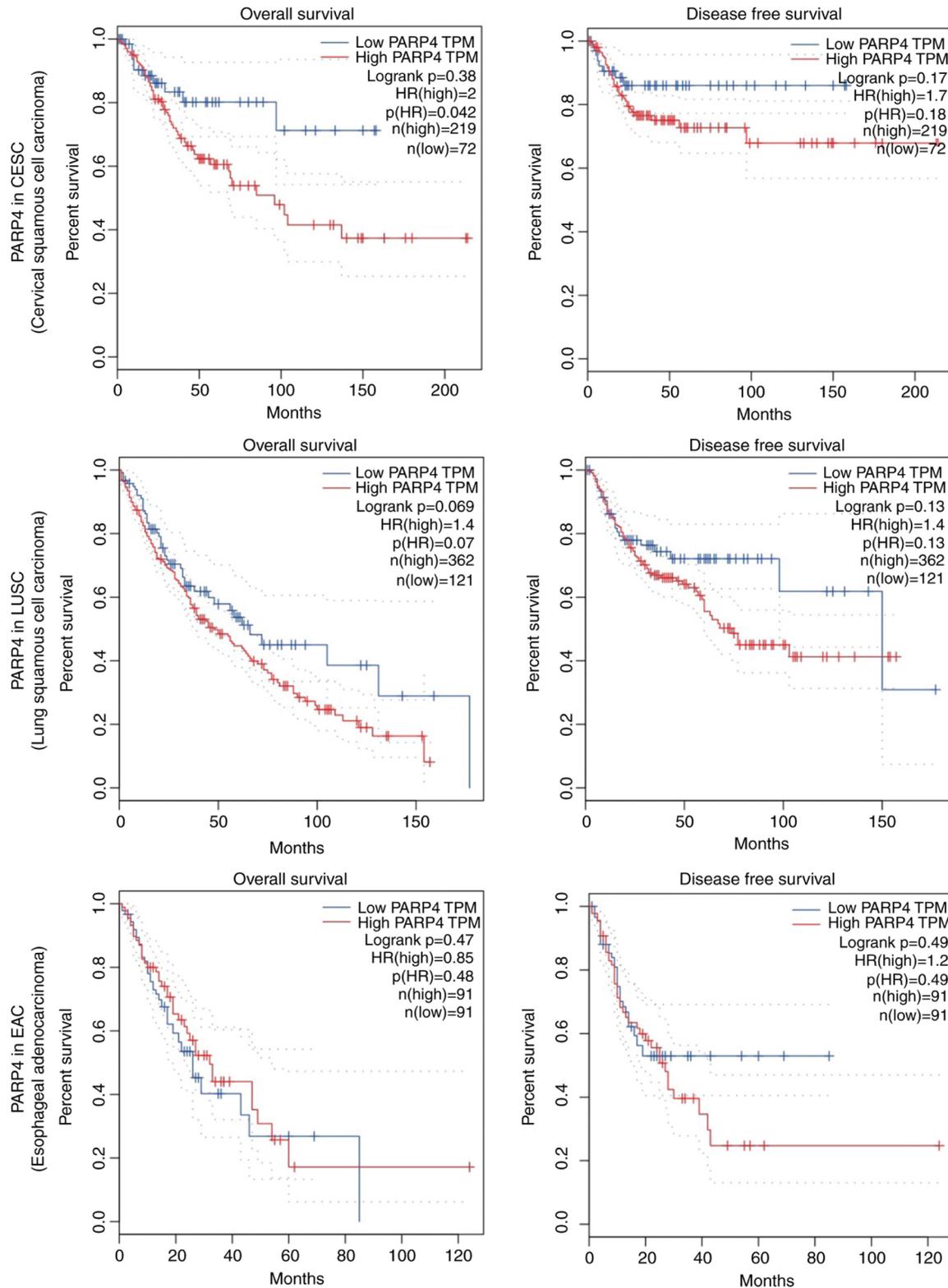


Figure S3. Expression level of PARP4 in the present ESCC cohort and its correlation with overall survival in patients. (A) Distribution of PARP4 with different IHC scores (from 0 to 3). (B) Correlation of different expression levels of PARP4 and overall survival in patients. poly(ADP-ribose) polymerase family member 4; ESCC, esophageal squamous cell carcinoma; IHC, immunohistochemical.

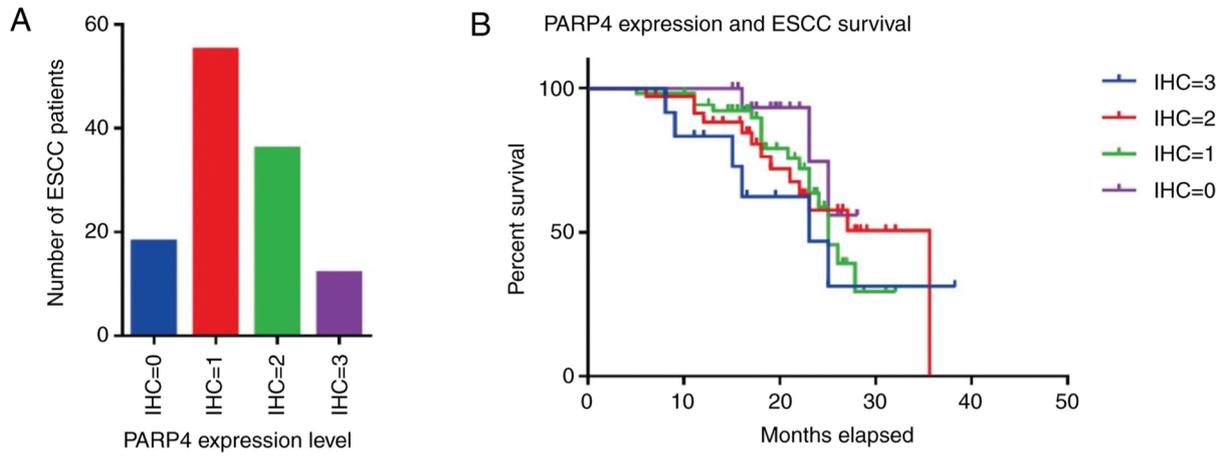


Table SI. List of stem cell markers used to calculate the SI.

Stemness-associated genes (SI)	Author, year	(Refs.)
EPHB2	Jung <i>et al</i> , 2011; Batlle <i>et al</i> , 2002	(1,2)
LATS2, CXCL2, MLLT10, METTL3, EZH2, VEGFA, EGFR, GPSM2, DNMT3A, HES1, MYC, RNF43, AXIN2, CDK6, RGMB, CDCA7, AQP1, DPP4, CFTR, TSPAN6, FERMT1, LRIG1, CA2, STMN1	Dalerba <i>et al</i> , 2011	(3)
ASCL2, OLFM4, LGR5, BMI1	Merlos-Suarez <i>et al</i> , 2011	(4)
SMOC2, ETS2, GPX2, FAM84A	Jung <i>et al</i> , 2015	(5)
PTPRG, SLC12A2		
SI, stemness index.		

Table SII. Genes responsible for esophageal adenocarcinoma stemness.

Symbol	Description	Author, year	(Refs.)
ACVR1B	Activin A receptor type 1B		
ALDH1A1	Aldehyde dehydrogenase 1 family member A1	Kulsum <i>et al</i> , 2017; Liu <i>et al</i> , 2016; Meng <i>et al</i> , 2014; Thomas <i>et al</i> , 2016; Yang <i>et al</i> , 2014	(6-10)
AURKA	Aurora kinase A	Chen <i>et al</i> , 2017; Eterno <i>et al</i> , 2016; Yang <i>et al</i> , 2017; Zheng <i>et al</i> , 2016	(11-14)
CENPJ	Centromere protein J		
FAM168A	Family with sequence similarity 168 member A		
GPR89B	G protein-coupled receptor 89B		
HMGB2	High mobility group box 2		
LANCL2	LanC like 2		
LONP2	Lon peptidase 2, peroxisomal		
PPP1R8	Protein phosphatase 1 regulatory subunit 8		
PTDSS1	Phosphatidylserine synthase 1		
RIF1	Replication timing regulatory factor 1	GursesCila <i>et al</i> , 2016; Li <i>et al</i> , 2015; Mei <i>et al</i> , 2017	(15-17)
SRSF8	Serine and arginine rich splicing factor 8		
STMN1	Stathmin 1	Li <i>et al</i> , 2017; Obayashi <i>et al</i> , 2017	(18,19)
TRIM59	Tripartite motif containing 59	Sang <i>et al</i> , 2018; Zhou <i>et al</i> , 2014	(20,21)
ZNF107	Zinc finger protein 107		

Table SIII. Genes responsible for esophageal squamous cell carcinoma stemness.

Symbol	Description	Author, year	(Refs.)
ANGEL2	Angel homolog 2		
APPBP2	Amyloid beta precursor protein binding protein 2		
BRD8	Bromodomain containing 8		
CDCA7	Cell division cycle associated 7	Guiu <i>et al</i> , 2014	(22)
CEP89	Centrosomal protein 89		
CUL7	Cullin 7		
DDX11	DEAD/H-box helicase 11		
ECHDC2	Enoyl-CoA hydratase domain containing 2		
FAM111A	Family with sequence similarity 111 member A		
FAM13A	Family with sequence similarity 13 member A		
FBXW2	F-box and WD repeat domain containing 2		
FGFR1OP	FGFR1 oncogene partner		
FN3KRP	Fructosamine 3 kinase related protein		
GAR1	GAR1 ribonucleoprotein		
GMCL1	Germ cell-less, spermatogenesis associated 1		
GNPDA1	Glucosamine-6-phosphate deaminase 1		
INTS4	Integrator complex subunit 4		
KIF11	kinesin family member 11	Imai <i>et al</i> , 2017; Jiang <i>et al</i> , 2017; Venere <i>et al</i> , 2015	(23-25)
MGAT1	Mannosyl (alpha-1,3-)-glycoprotein beta-1,2-N- acetylglucosaminyltransferase		
MPP1	Membrane palmitoylated protein 1		
NBPF1	Neuroblastoma breakpoint family member 1		
OGFOD3	2-oxoglutarate and iron dependent oxygenase domain containing 3		
PAK1IP1	PAK1 interacting protein 1		
PARP4	Poly(ADP-ribose) polymerase family member 4		
PRIM2	Primase (DNA) subunit 2		
RAD17	RAD17 checkpoint clamp loader component		
SNIP1	Smad nuclear interacting protein 1		
TPRA1	Transmembrane protein adipocyte associated 1		
TRAF5	TNF receptor associated factor 5		
USP11	Ubiquitin specific peptidase 11		
WDR92	WD repeat domain 92		
WLS	Wntless Wnt ligand secretion mediator	Augustin <i>et al</i> , 2017; Augustin <i>et al</i> , 2016	(26,27)
ZADH2	Zinc binding alcohol dehydrogenase domain containing 2		
ZMYM2	Cinc finger MYM-type containing 2	Ren <i>et al</i> , 2011; Ren <i>et al</i> , 2016	(28,29)
ZNF761	Zinc finger protein 761		

Table SIV. Patients' information and PARP4 expression in our ESCC cohort.

Patient ID	Diagnosis age	Sex	Cancer type	American Joint Committee on Cancer Tumor Stage Code	Neoplasm Disease Lymph Node Stage American Joint Committee on Cancer Code	Vital status	OS_time (Months)	IHC score for PARP4
201200100	77	Female	Esophageal squamous cell carcinoma	T3	N2	Dead	23.00	1
201200101	71	Male	Esophageal squamous cell carcinoma	T3	N3	Dead	8.00	3
201200426	66	Male	Esophageal squamous cell carcinoma	T4	N2	Dead	17.00	1
201200428	58	Female	Esophageal squamous cell carcinoma	T1	N0	Alive	18.50	1
201200562	63	Male	Esophageal squamous cell carcinoma	T2	N1	Alive	26.50	1
201200638	69	Male	Esophageal squamous cell carcinoma	T1	N1	Alive	15.80	2
201200640	60	Male	Esophageal squamous cell carcinoma	T4	N2	Dead	16.00	3
201200878	62	Female	Esophageal squamous cell carcinoma	T1	N0	Alive	22.60	2
201200905	65	Female	Esophageal squamous cell carcinoma	T3	N2	Dead	19.00	2
201200907	63	Male	Esophageal squamous cell carcinoma	T4	N3	Dead	18.00	1
201200911	68	Male	Esophageal squamous cell carcinoma	T3	N2	Dead	16.00	2
201201066	53	Male	Esophageal squamous cell carcinoma	T2	N1	Alive	19.00	0
201201187	60	Male	Esophageal squamous cell carcinoma	T4	N1	Alive	28.00	0
201201480	71	Male	Esophageal squamous cell carcinoma	T2	N1	Alive	38.20	3
201201689	47	Female	Esophageal squamous cell carcinoma	T1	N0	Alive	17.50	1
201202134	64	Female	Esophageal squamous cell carcinoma	T2	N2	Alive	14.90	1
201202137	63	Male	Esophageal squamous cell carcinoma	T1	N0	Alive	15.60	0
201202138	66	Male	Esophageal squamous cell carcinoma	T4	N3	Dead	27.80	1
201202143	68	Male	Esophageal squamous cell carcinoma	T3	N0	Alive	16.80	2
201202232	58	Male	Esophageal squamous cell carcinoma	T2	N2	Alive	12.50	1
201202233	62	Male	Esophageal squamous cell carcinoma	T3	N2	Alive	23.80	1
201202347	66	Male	Esophageal squamous cell carcinoma	T4	N1	Alive	25.00	3
201202351	68	Male	Esophageal squamous cell carcinoma	T3	N3	Dead	15.00	3
201202354	72	Male	Esophageal squamous cell carcinoma	T4	N2	Dead	25.00	3
201202478	64	Female	Esophageal squamous cell carcinoma	T3	N1	Dead	18.00	1
201202481	60	Male	Esophageal squamous cell carcinoma	T1	N0	Alive	24.10	1
201202486	60	Female	Esophageal squamous cell carcinoma	T2	N1	Alive	26.90	1
201202492	50	Female	Esophageal squamous cell carcinoma	T3	N3	Dead	26.00	1
201202500	72	Female	Esophageal squamous cell carcinoma	T4	N2	Dead	23.00	3
201202562	69	Male	Esophageal squamous cell carcinoma	T2	N1	Alive	27.80	2
201202573	58	Male	Esophageal squamous cell carcinoma	T4	N3	Dead	21.00	2
201202588	60	Male	Esophageal squamous cell carcinoma	T1	N1	Alive	8.00	2
201202591	59	Female	Esophageal squamous cell carcinoma	T3	N0	Dead	13.00	1
201202594	52	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	28.00	2
201202680	57	Female	Esophageal squamous cell carcinoma	T1	N2	Alive	29.00	2
201202684	81	Male	Esophageal squamous cell carcinoma	T2	N2	Alive	31.00	2

Table SIV. Continued.

Patient ID	Diagnosis age	Sex	Cancer type	American Joint Committee on Cancer Tumor Stage Code	Neoplasm Disease Lymph Node Stage American Joint Committee on Cancer Code	Vital status	OS_time (Months)	IHC score for PARP4
201202954	69	Female	Esophageal squamous cell carcinoma	T1	N1	Alive	32.00	2
201202960	60	Male	Esophageal squamous cell carcinoma	T1	N3	Alive	14.00	2
201202961	20	Female	Esophageal squamous cell carcinoma	T2	N0	Alive	13.00	2
201202963	58	Male	Esophageal squamous cell carcinoma	T3	N1	Dead	24.00	1
201203039	58	Male	Esophageal squamous cell carcinoma	T4	N0	Dead	18.00	1
201203040	64	Male	Esophageal squamous cell carcinoma	T2	N2	Alive	15.00	0
201203043	66	Female	Esophageal squamous cell carcinoma	T1	N3	Alive	16.50	1
201203044	75	Female	Esophageal squamous cell carcinoma	T2	N2	Alive	18.50	1
201203145	70	Male	Esophageal squamous cell carcinoma	T4	N1	Alive	22.00	1
201203225	61	Male	Esophageal squamous cell carcinoma	5	N1	Alive	23.50	1
201203298	65	Male	Esophageal squamous cell carcinoma	T2	N2	Alive	24.60	1
201203301	62	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	22.30	2
201203302	45	Male	Esophageal squamous cell carcinoma	T3	N0	Alive	28.40	2
201203324	57	Male	Esophageal squamous cell carcinoma	T3	N0	Alive	17.50	0
201203325	64	Male	Esophageal squamous cell carcinoma	T1	N1	Alive	22.00	0
201203406	70	Female	Esophageal squamous cell carcinoma	T1	N2	Alive	32.00	1
201203408	60	Female	Esophageal squamous cell carcinoma	T1	N3	Alive	12.00	2
201203415	68	Male	Esophageal squamous cell carcinoma	T1	N0	Alive	18.00	1
201203416	56	Male	Esophageal squamous cell carcinoma	T2	N1	Alive	14.50	1
201203427	70	Male	Esophageal squamous cell carcinoma	T2	N0	Alive	16.80	1
201203507	62	Male	Esophageal squamous cell carcinoma	T3	N2	Dead	25.00	1
201203594	72	Female	Esophageal squamous cell carcinoma	T3	N3	Alive	18.40	1
201203611	66	Male	Esophageal squamous cell carcinoma	T3	N0	Dead	25.00	1
201203700	71	Female	Esophageal squamous cell carcinoma	T3	N1	Alive	19.60	1
201203714	50	Male	Esophageal squamous cell carcinoma	T3	N2	Dead	23.00	2
201203807	72	Male	Esophageal squamous cell carcinoma	T2	N3	Alive	22.00	1
201204016	47	Male	Esophageal squamous cell carcinoma	T3	N3	Alive	21.50	1
201204030	76	Male	Esophageal squamous cell carcinoma	T2	N2	Dead	16.00	0
201204032	57	Female	Esophageal squamous cell carcinoma	T2	N3	Alive	22.50	1
201204033	68	Male	Esophageal squamous cell carcinoma	T3	N0	Alive	26.50	2
201204113	48	Female	Esophageal squamous cell carcinoma	T2	N1	Alive	28.70	1
201204114	60	Female	Esophageal squamous cell carcinoma	T3	N2	Alive	26.40	0
201204382	70	Female	Esophageal squamous cell carcinoma	T4	N3	Alive	26.00	0
201204392	60	Male	Esophageal squamous cell carcinoma	T4	N0	Alive	21.00	0
201204400	45	Female	Esophageal squamous cell carcinoma	T4	N1	Alive	20.00	0
201204446	69	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	19.00	2

Table SIV. Continued.

Patient ID	Diagnosis age	Sex	Cancer type	American Joint Committee on Cancer Tumor Stage Code	Neoplasm Disease Lymph Node Stage American Joint Committee on Cancer Code	Vital status	OS_time (Months)	IHC score for PARP4
201204454	67	Female	Esophageal squamous cell carcinoma	T3	N1	Dead	11.00	1
201204467	61	Male	Esophageal squamous cell carcinoma	T3	N0	Alive	18.00	1
201204470	74	Female	Esophageal squamous cell carcinoma	T3	N2	Alive	17.00	0
201204562	69	Female	Esophageal squamous cell carcinoma	T3	N2	Alive	15.00	0
201204564	66	Male	Esophageal squamous cell carcinoma	T2	N0	Alive	16.00	1
201204569	74	Male	Esophageal squamous cell carcinoma	T2	N1	Alive	14.50	1
201204622	63	Male	Esophageal squamous cell carcinoma	T2	N0	Alive	15.50	1
201204630	75	Male	Esophageal squamous cell carcinoma	T2	N2	Dead	17.00	2
201204707	74	Male	Esophageal squamous cell carcinoma	T2	N0	Alive	16.50	2
201204727	71	Male	Esophageal squamous cell carcinoma	T1	N1	Alive	17.50	1
201204738	64	Female	Esophageal squamous cell carcinoma	T3	N0	Dead	5.00	1
201204820	63	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	19.50	0
201204914	59	Male	Esophageal squamous cell carcinoma	T4	N3	Alive	17.50	0
201204928	60	Female	Esophageal squamous cell carcinoma	T4	N0	Dead	23.00	0
201205040	48	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	19.60	0
201205095	69	Male	Esophageal squamous cell carcinoma	T2	N0	Alive	18.50	1
201205113	69	Male	Esophageal squamous cell carcinoma	T3	N2	Dead	25.00	0
201205176	62	Female	Esophageal squamous cell carcinoma	T2	N0	Alive	17.50	2
201205183	67	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	11.00	2
201205184	72	Male	Esophageal squamous cell carcinoma	T3	N0	Dead	22.00	2
201205190	62	Female	Esophageal squamous cell carcinoma	T1	N1	Alive	12.00	3
201205268	77	Male	Esophageal squamous cell carcinoma	T4	N2	Dead	9.00	3
201205277	64	Male	Esophageal squamous cell carcinoma	T4	N3	Alive	13.00	1
201205278	75	Female	Esophageal squamous cell carcinoma	T1	N0	Alive	14.00	2
201205285	55	Male	Esophageal squamous cell carcinoma	T3	N2	Dead	11.00	2
201205286	63	Male	Esophageal squamous cell carcinoma	T4	N3	Dead	11.00	1
201205294	49	Female	Esophageal squamous cell carcinoma	T2	N0	Alive	19.50	3
201205547	68	Female	Esophageal squamous cell carcinoma	T3	N1	Alive	7.00	1
201205562	59	Male	Esophageal squamous cell carcinoma	T4	N0	Alive	6.00	1
201205584	58	Male	Esophageal squamous cell carcinoma	T1	N3	Alive	16.50	3
201205770	76	Male	Esophageal squamous cell carcinoma	T3	N0	Alive	26.50	2
201206004	68	Male	Esophageal squamous cell carcinoma	T3	N3	Dead	18.00	1
201206074	63	Male	Esophageal squamous cell carcinoma	T3	N2	Dead	27.00	2
201206075	69	Female	Esophageal squamous cell carcinoma	T1	N0	Alive	8.00	1
201206217	73	Male	Esophageal squamous cell carcinoma	T1	N1	Dead	18.00	2
201206231	56	Male	Esophageal squamous cell carcinoma	T2	N2	Dead	12.00	2

Table SIV. Continued.

Patient ID	Diagnosis age	Sex	Cancer type	American Joint Committee on Cancer Tumor Stage Code	Neoplasm Disease Lymph Node Stage American Joint Committee on Cancer Code	Vital status	OS_time (Months)	IHC score for PARP4
201206239	60	Female	Esophageal squamous cell carcinoma	T1	N1	Dead	23.00	1
201206321	60	Male	Esophageal squamous cell carcinoma	T3	N1	Alive	7.00	2
201206336	54	Male	Esophageal squamous cell carcinoma	T2	N2	Dead	22.00	1
201206356	68	Male	Esophageal squamous cell carcinoma	T1	N3	Alive	15.00	1
201206436	57	Male	Esophageal squamous cell carcinoma	T1	N3	Alive	24.00	1
201206439	55	Male	Esophageal squamous cell carcinoma	T2	N2	Alive	26.00	2
201206442	62	Female	Esophageal squamous cell carcinoma	T3	N1	Dead	20.80	1
201206443	62	Male	Esophageal squamous cell carcinoma	T4	N0	Alive	31.00	1
201206516	62	Male	Esophageal squamous cell carcinoma	T3	N2	Alive	11.00	3
201206628	55	Male	Esophageal squamous cell carcinoma	T2	N3	Alive	10.00	1
201206632	71	Male	Esophageal squamous cell carcinoma	T2	N0	Dead	11.00	2
201206731	59	Male	Esophageal squamous cell carcinoma	T1	N1	Alive	35.57	2
201206738	62	Male	Esophageal squamous cell carcinoma	T1	N1	Dead	6.00	2

IHC, immunohistochemical.

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