Figure S1. Differences of PD-L1 mRNA expression and PD-1 mRNA expression between head and neck tumors and normal tissues. PD-L1 mRNA expression estimated by unpaired t test (A) and paired t test (B). PD-L1 mRNA expression is upregulated in tumors compared with para-tumor normal tissues. P=0.0363 and P=0.0584, respectively. PD-1 mRNA expression indicated no significant difference between tumors and normal tissues (C-D). P=0.2724 and P=0.3713, respectively.
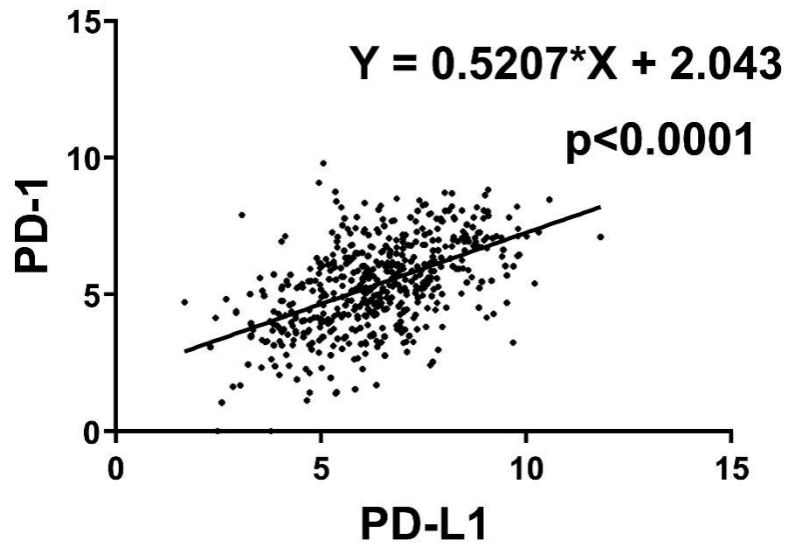
Correlation of PD-L1 and PD-1

$$Y = 0.5207 * X + 2.043$$

$$p < 0.0001$$

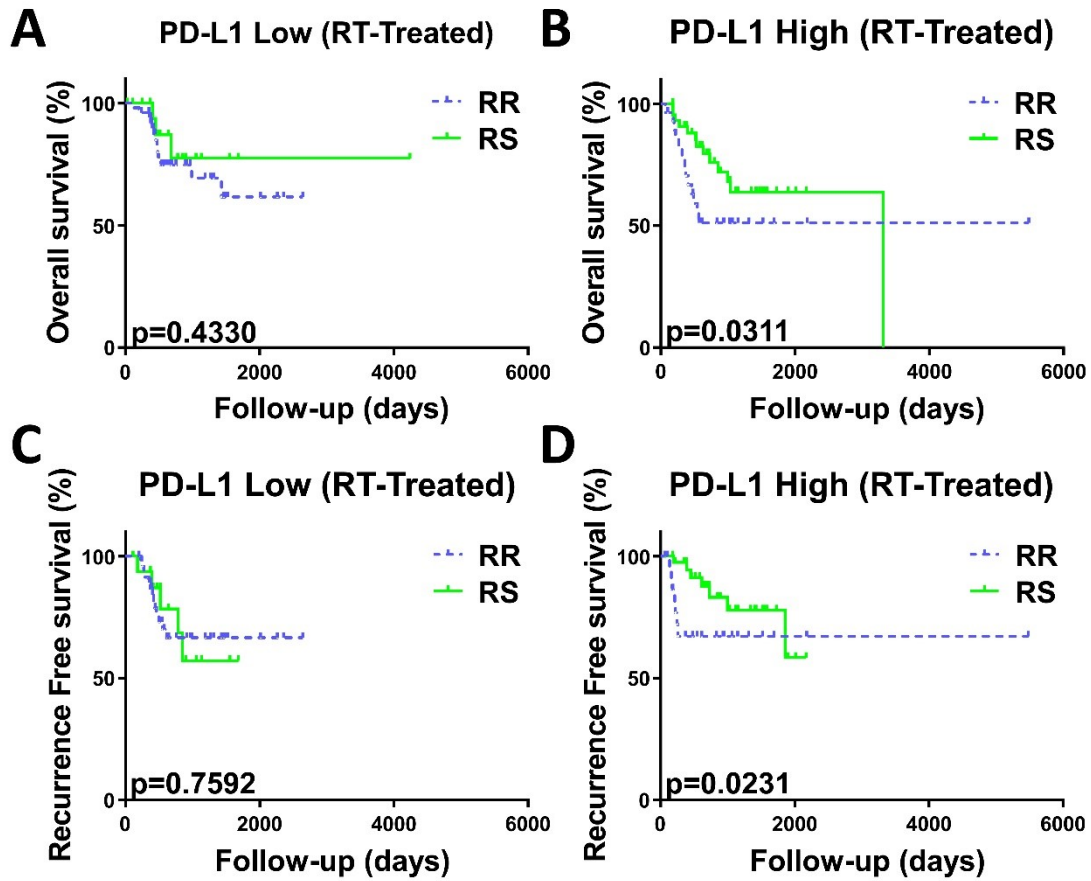Figure S2. Correlations of PD-L1 mRNA with PD-1 mRNA expression. P<0.0001.

Figure S3. Kaplan-Meier curves analysis stratified by PD-L1 expression level. OS curve (B) and RFS curve (D) indicated worse prognosis of patients with the RR gene signature in the high PD-L1 mRNA group compared with RS. P=0.0311 and 0.0231, respectively. OS curves (A) and RFS curve (C) indicated no significant difference between patients with RR and RS gene signatures in the low PD-L1 mRNA group. P=0.4330 and 0.7592, respectively. P-values calculated using the Gehan-Breslow-Wilcoxon test.

Table S1.Univariate analysis for overall survival (OS) and recurrence-free survival (RFS) according to PD-L1 level

| | OS | | | | | | | | | RFS | | | | | | | | |
| | Low | | | High | | | Overall | | | Low | | | High | | | Overall | | |
	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value
Age																		
<60	1			1			1			1			1			1		
>=60	0.95	0.35-2.54	0.809	2.21	1.0-4.85	0.051	1.72	0.93-3.14	0.083	1.28	0.51-3.22	0.588	1.76	0.61-5.06	0.214	1.55	0.77-3.09	0.161
Margin status																		
Positive	1			1			1			1			1			1		
Negative or	0.20	0.06-0.71	**0.028**	2.84	0.25-32.81	0.410	0.45	0.16-1.27	0.228	0.37	0.11-1.22	0.150	2.847	0.13-60.08	0.506	0.42	0.13-1.30	0.263
HPV																		
Positive				1			1			1			1			1		
Negative	3.04	0.004-2089	0.739	3.72	0.40-34.97	0.254	3.41	0.50-23.21	0.2204	3.04	0.004-2089	0.739	0.15	0.004-4.92	0.814	1.01	0.12-8.78	0.523
P16																		
Positive				1			1			1			1			1		
Negative	4.01	0.16-100.1	0.502	1.84	0.30-11.21	0.546	2.08	0.42-10.17	0.435	3.269	0.13-82.68	0.491	0.33	0.01-7.52	>0.999	1.36	0.18-10.19	0.433
Stage																		
I to III				1			1			1			1			1		
IV	1.15	0.27-4.84	0.604	3.98	1.57-10.09	**0.013**	2.53	1.17-5.477	**0.031**	2.19	0.59-8.10	0.308	1.39	0.45-4.25	0.797	1.72	0.76-3.90	0.428
Radiosensitivity																		
RR	1			1			1			1			1			1		
RS	0.66	0.22-2.01	0.433	0.49	0.21-1.10	**0.019**	0.65	0.35-1.21	0.075	1.01	0.35-2.83	0.759	0.44	0.14-1.35	**0.023**	0.67	0.33-1.33	0.057
PD-L1																		
low							1									1		
high							1.45	0.78-2.67	0.177							0.78	0.39-1.55	0.650

a. Gehan-Breslow-Wilcoxon tests

Abbreviations: HPV, HPV status assessed by ISH testing; P16, HPV status assessed by p16 testing; RR, radioresistant group; RS, radiosensitive group

Table S2. Univariate analysis for overall survival (OS) and recurrence-free survival (RFS) according to PD-1 level

	OS									RFS								
	Low			High			Overall			Low			High			Overall		
	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value	HR	95%CI	P-value
Age																		
<60	1						1			1						1		
>=60	1.07	0.51-2.25	0.982[a]	1.71	0.68-4.29	0.348	1.33	0.75-2.37	0.531	0.63	0.25-1.55	0.424	1.33	0.38-4.68	0.441	0.86	0.42-1.79	0.891
Margin status																		
Positive	1						1			1						1		
Negative or Close	0.18	0.06-0.52	**0.009**	1.25	0.20-7.79	0.837	0.28	0.11-0.71	**0.010**	0.44	0.12-1.55	0.159	3.00	0.21-41.51	0.442	0.51	0.15-1.66	0.207
HPV																		
Positive	1						1			1						1		
Negative	-[b]	-	-	5.19	0.60-44.53	0.131	4.05	0.73-22.63	0.120	-	-	-	0.08	0.004-1.36	0.134	0.30	0.03- 2.79	0.510
P16																		
Positive	1						1			1						1		
Negative	0.75	0.07-8.03	0.554	7.89	1.07-58.19	**0.042**	3.429	0.95-12.32	0.099	3.308	0.21-52.26	0.404	0.16	0.02-1.62	0.176	1.00	0.22-4.50	0.489
Stage																		
I to III	1						1			1						1		
IV	1.88	0.67-5.27	0.243	2.22	0.71-6.90	0.117	1.99	0.95-4.17	**0.041**	2.42	0.70-8.39	0.127	0.64	0.13-3.10	0.642	1.61	0.63-4.12	0.260
Radiosensitivity																		
RR	1						1			1						1		
RS	0.96	0.13-6.87	0.941	0.37	0.05-2.70	0.229	0.66	0.37-1.17	0.071	4.233	0.47-37.77	0.225	2.89	0.20-42.58	0.472	0.68	0.33-1.40	0.152
PDL1																		
low							1									1		
high							0.68	0.38-1.21	0.128							0.49	0.24-1.02	**0.023**

a. Gehan-Breslow-Wilcoxon tests

b. An insufficient number of cases

Abbreviations: HPV, HPV status assessed by ISH testing; P16, HPV status assessed by p16 testing; RR, radioresistant group; RS, radiosensitive group.

Table S3. Cox hazard regression models for overall survival (OS) and recurrence-free survival (RFS) based on PD-L1 and PD-1 levels

		OS			RFS		
		HR	95%CI	P-value	HR	95%CI	P-value
PD-L1							
PD-L1 Low							
Margin status	Positive(vs.Negative/Close)	5.89	1.92-18.09	**0.002**	2.57	0.81-8.17	0.11
Radiosensitivity	RR(vs.RS)	4.78	0.98-23.39	0.053	1.3	0.39-4.36	0.672
PD-L1 High							
Stage	I to IV (Incremental)	12.34	1.60-94.84	**0.016**	1.39	0.65-2.97	0.393
Radiosensitivity	RR(vs.RS)	3.68	1.43-9.49	**0.007**	2.56	0.83-7.91	0.102
Overall							
Stage	I to IV (Incremental)	3.45	1.18-10.14	**0.024**	1.51	0.79-2.90	0.21
Radiosensitivity	RR(vs.RS)	2.01	0.97-4.49	0.06	1.36	0.63-2.91	0.429
PD-1							
PD-1 Low							
Margin status	Positive(vs.Negative/Close)	4.23	1.76-10.18	**0.001**	1.61	0.45-5.82	0.464
Radiosensitivity	RR(vs.RS)	2.61	0.33-20.77	0.365	0.55	0.09-3.34	0.516
Overall							
Margin status	Positive(vs.Negative/Close)	2.54	1.20-5.38	**0.018**	1.28	0.42-3.93	0.668
Stage	I to IV (Incremental)	1.36	0.77-2.40	0.293	1.08	0.57-2.05	0.815
PD-1	High(vs.Low)	1.07	0.80-1.47	0.65	0.66	0.47-0.93	**0.018**
Radiosensitivity	RR(vs.RS)	1.86	0.51-6.82	0.35	0.29	0.07-1.28	0.102

Abbreviations: HPV, HPV status assessed by ISH testing; P16, HPV status assessed by p16 testing; RR, radioresistant group; RS, radiosensitive group

Table S4. Recent studies concerning PD-L1 and PD-1 in HNCs

Author Journal Year	DOI	Patient	Tumor Location	Treatment	Method	Correlates for radiosensitivity and HPV	Correlates for prognosis
Fiedler, M. Clin Oral Investig 2018	10.1007/s00784-017-2099-x	82	HNSCC	65 patients (79.3%): concurrent chemoradiotherapy (CRT), 17 patients (20.7%): RT	PD-L1: Immunohistochemistry PD-1+TILs: Immunohistochemistry	High PD-L1 indicated radiosensitive	High PD-1 was correlated with reduced risk for local recurrence
Muller, T. Oncotarget 2017	10.18632/oncotarget.17547	293	HNSCC	Surgery with optional adjuvant radiochemotherapy or definitive radio-chemotherapy with curative intent	PD-L1: Immunohistochemistry		High PD-L1 was associated with worse overall survival
Garcia-Pedrero, J. M. J Am Acad Dermatol 2017	10.1016/j.jaad.2017.05.047	100	Cutaneous squamous cell (cSCC) carcinoma of the head and neck	No adjuvant therapy after surgery	PD-L1: Immunohistochemistry		High PD-L1 predicts increased risk for nodal metastasis
Lin, Y. M. PLoS One 2015	10.1371/journal.pone.0	305	OSCC	-	PD-L1: Immunohistochemistry		High PD-L1 was an independent risk factor of overall survival in males and smokers

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Birtalan, E. Appl Immunohistochem Mol Morphol 2017	10.10 97/pai .0000 00000 00000 590	106	Laryngeal, Oropharyn geal, and Hypophary ngeal Cancer	Surgery: 41.5%; Chemoradiation: 18.9%; Radiation: 19.8%; Induction chemotherapy: 32.1%; Chemotherapy: 0.9%; Chemotherapy plus biological therapy: 3.8%; Radiation plus biological therapy: 0.9%	PD-L1: Immunohistochemistry		High PD-L1 expression on immune cells was associated with better disease-specific survival in HPV-negative tumors and laryngeal tumors.
Vassilakopoulou, M. Clin Cancer Res 2016	10.11 58/10 78-04 32.CC R-15-1 543	238	primary laryngeal SCCs	Potentially curative resection with or without external beam irradiation	PD-L1: automated quantitative protein analysis (AQUA)		High PD-L1 AQUA levels were significantly associated with superior disease-free survival and overall survival
Balermpas, P. Int. J. Cancer 2017	10.10 02/ijc. 30770	161	oropharyn x, hypophary nx or oral cavity	Surgery and postoperative cisplatin-based CRT	PD-L1: Immunohistochemistry PD-1⁺TILs:Immunohisto chemistry		High PD-L1 expression correlated with superior OS, LPFS and DMFS in oropharynx.High PD-1 expression in the intratumoral compartment exhibited a significantly positive correlation with OS,LPFS and DMFS.
Kansy, B. A. Cancer Res	10.11 58/00	HPV: 26	HNSCC	-	PD-1+ TIL: flow cytometry analysis	PD-1 + TIL was increased in	Increased PD-1 high CD8 + TILscorrelated with significantly

| 2017 | 08-5472.can-16-3167 | CD8 + TIL:56 | | | | HPV-positive patients who experienced better clinical outcome. | worse disease-free survival (DFS) and increased hazard ratio for recurrence, whereas increased PD-1 low T cells was associated with HPV positivity and better outcome. |

Table S5 The 31-genes signature related to radiosensitivity

	Downregulated in radioresistant (RR) cells	Upregulated in radioresistant (RR) cells
Symbol	ARHGDIB, CORO1A, CXCR4, HCLS1, LAPTM5, LRMP, MYB, PTPRC, PTPRCAP, WAS	ACTN1, ANXA2, ANXA5, CAPNS1, CBR1, CCND1, CD63, DAG1, EMP2, HTRA1, ITGB5, PFN2, PIR, PKM2, PTMS, PYGB, RAB13, RALB, SCRN1, SQSTM1, TWF1