

Supplementary table 1: Patient characteristics including demographic and tumor-related parameters

(n=49).

Patient characteristics		
Age (years)		
Median	60	
Minimum	34	
Maximum	78	
Gender		
	n	%
Male	44	89.8
Female	5	10.2
Tumor location		
Oral cavity	2	4.1
Oropharynx	19	38.8
Hypopharynx	12	24.5
Larynx	7	14.3
Multi-level	9	18.4
Tumor extent		
T1	1	2.0
T2	4	8.2
T3	14	28.6
T4	30	61.2
Nodal status		
N0	4	8.2
N1	1	2.0
N2a	0	0.0
N2b	9	18.4
N2c	35	71.4
HPV status		
HPV positive	9	18.4
HPV negative	40	81.6

Abbreviations: HPV=human papillomavirus

Supplementary table 2: Description of antibodies used for immunohistochemical stains and corresponding antigen retrieval.

Antigen	Clone	Company	Dilution	Antigen retrieval
PD-1	NAT105	Roche/Ventana	Prediluted	Tris-EDTA buffer pH 9
PD-L1	SP263	Roche/Ventana	Prediluted	Tris-EDTA buffer pH 9
CAIX	C48E	Cell Signaling	1:300	pH 6.1 citrate buffer
CD34	QBEnd10 (IR632)	DAKO	Prediluted	pH 6.1 citrate buffer
HIF1 α	MAB1935	R&D	1:100	pH 6.1 citrate buffer

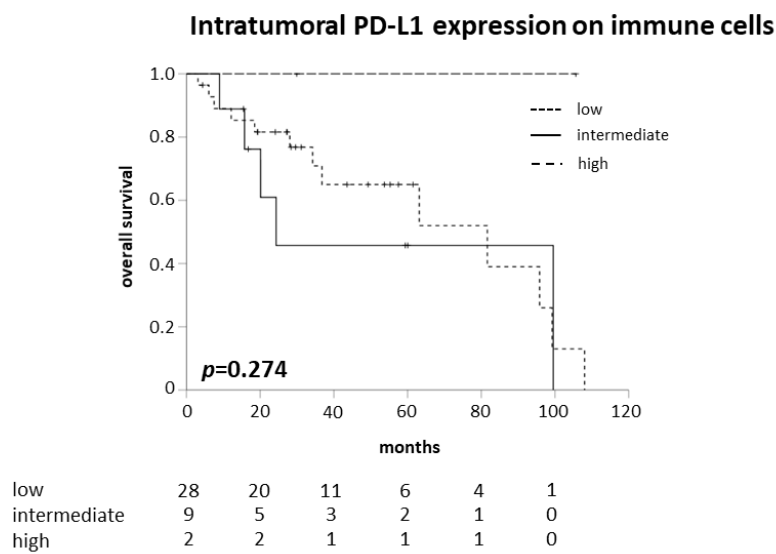
Supplementary table 3: Tests for potential differences regarding the PD-1 and PD-L1 expression (including the tumoral PD-L1 expression [TPS]) depending on the HPV status. *P* values of the appropriate tests are indicated.

		PD-1 tumor	PD-1 stromal	PD-L1 tumor	PD-L1 stromal	TPS
HPV status	p	0.805 ¹	0.589 ¹	0.718 ²	0.582 ²	0.635 ²

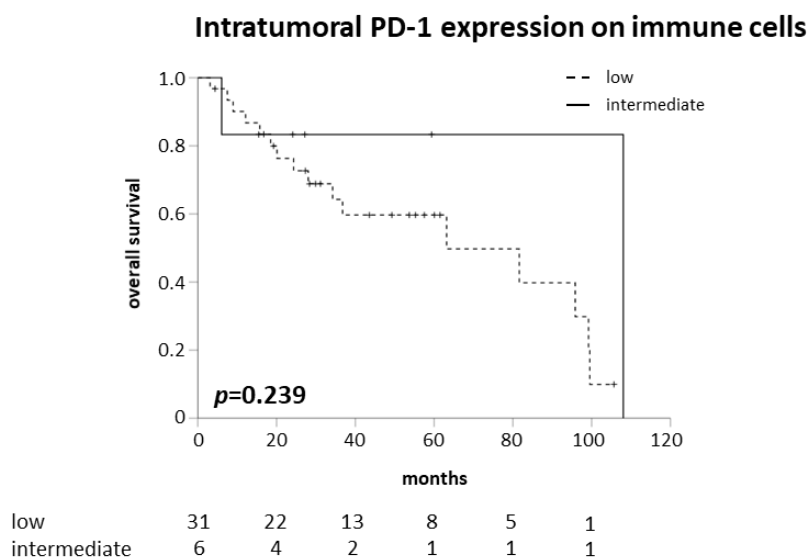
¹ Chi-square test, ² Mann-Whitney-U test

Supplementary figure 1. OS in HNSCC patients undergoing chemoradiation is independent from pre-therapeutic PD-L1 and PD-1 expression on intratumoral immune cells. OS of HNSCC patients receiving chemoradiation stratified by PD-L1 (A) and PD-1 (B) expression. *P* values are derived from log-rank tests.

A

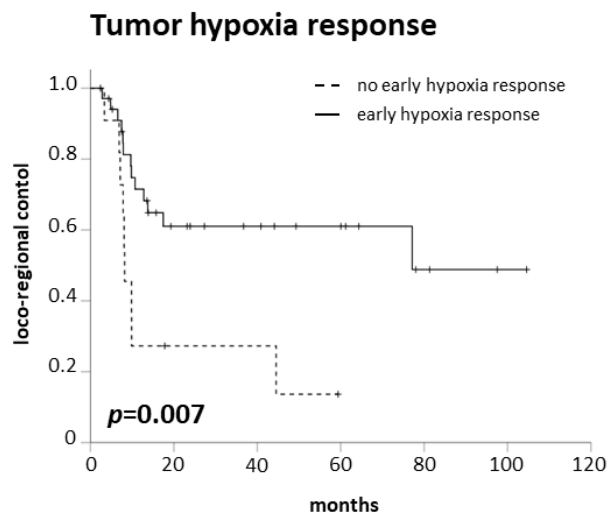


B



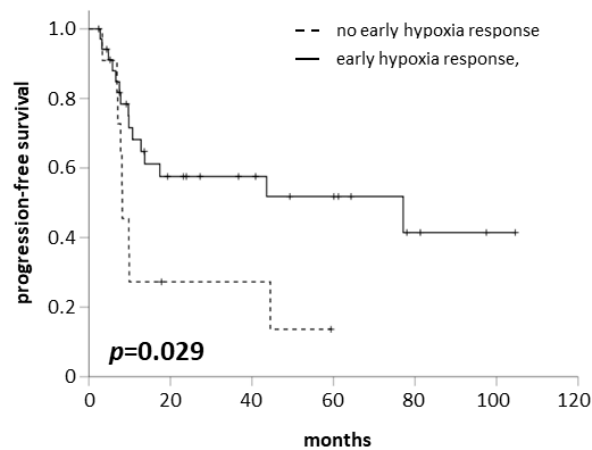
Supplementary figure 2. Early hypoxia response leads to improved LRC and PFS in HNSCC patients receiving definitive chemoradiation. LRC (A) and PFS (B) of HNSCC patients stratified by tumor hypoxia resolution between week 0 and 2 of chemoradiation. *P* values are derived from log-rank tests.

A



no early hypoxia response	11	2	2	0	0	0
early hypoxia response	35	15	11	8	3	1

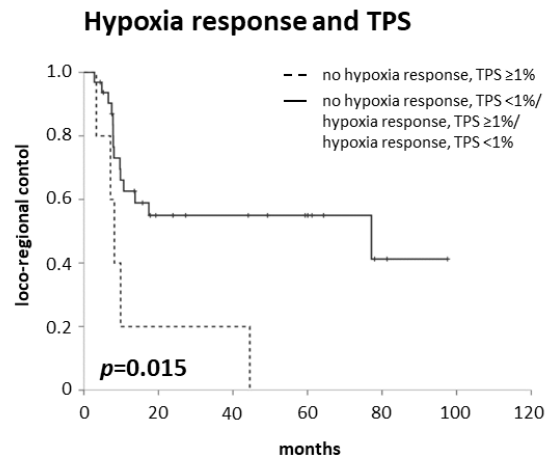
B



no early hypoxia response	11	2	2	0	0	0
early hypoxia response	35	15	11	8	3	1

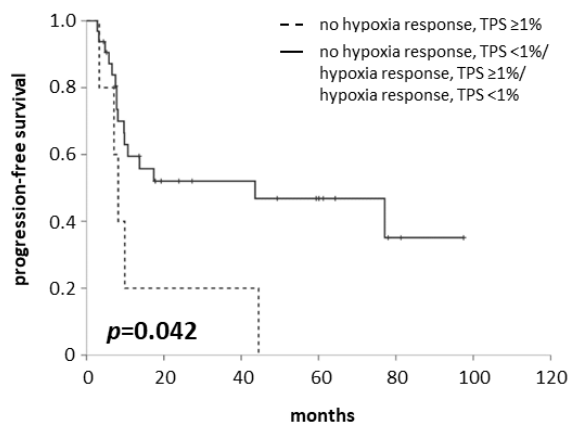
Supplementary figure 3. Persistent tumor-associated hypoxia and high TPS result in worse LRC and PFS. LRC (A) and PFS (B) of HNSCC patients with missing early hypoxia resolution (between weeks 0 and 2) and high TPS compared to the remaining patients with either present early hypoxia resolution or low TPS. *P* values are derived from log-rank tests.

A



no hypoxia response, TPS $\geq 1\%$	5	1	1	0	0	0
no hypoxia response, TPS $< 1\%$ / hypoxia response, TPS $\geq 1\%$ / hypoxia response, TPS $< 1\%$	32	12	10	7	2	0

B



no hypoxia response, TPS $\geq 1\%$	5	1	1	0	0	0
no hypoxia response, TPS $< 1\%$ / hypoxia response, TPS $\geq 1\%$ / hypoxia response, TPS $< 1\%$	32	12	10	7	2	0