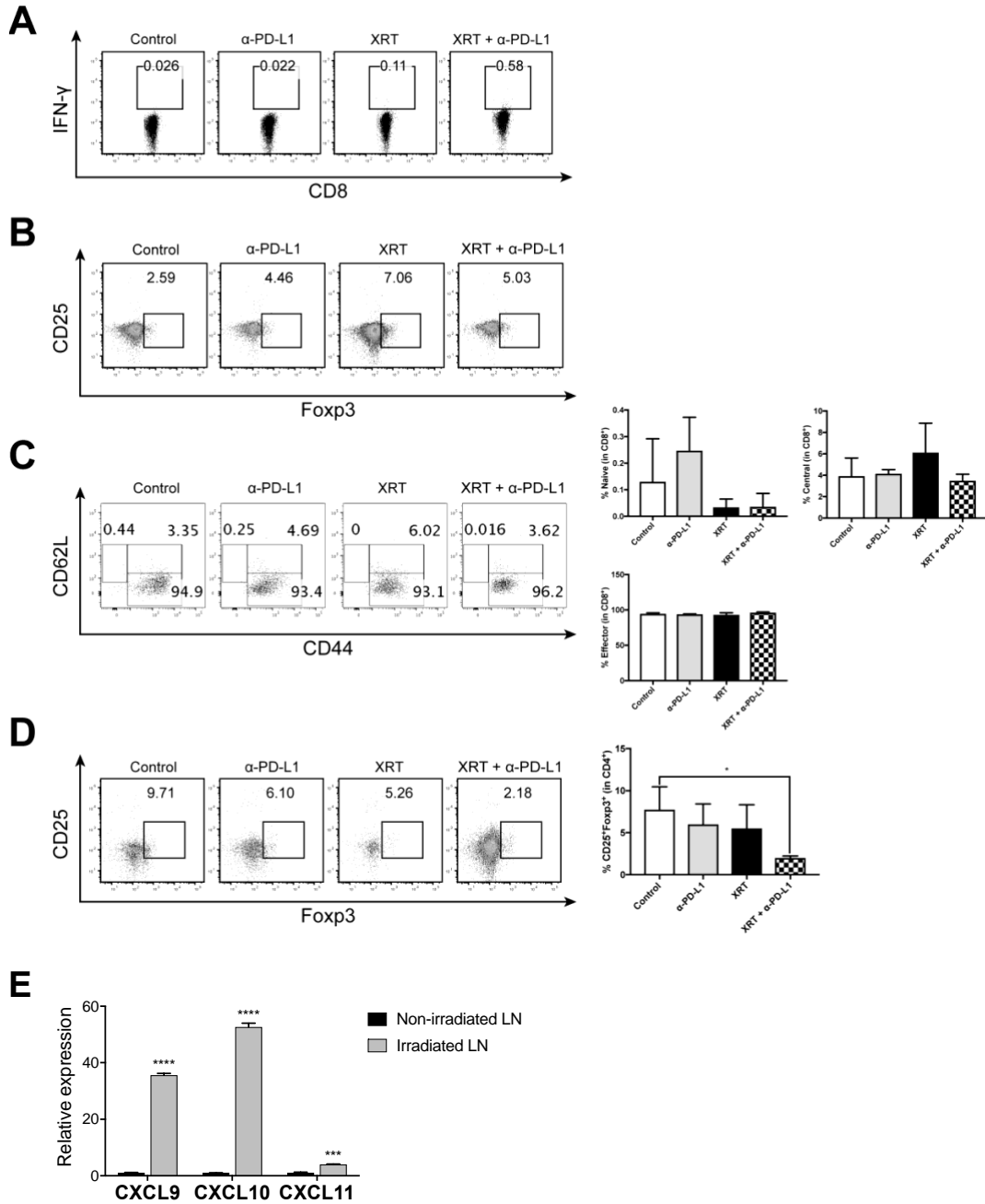
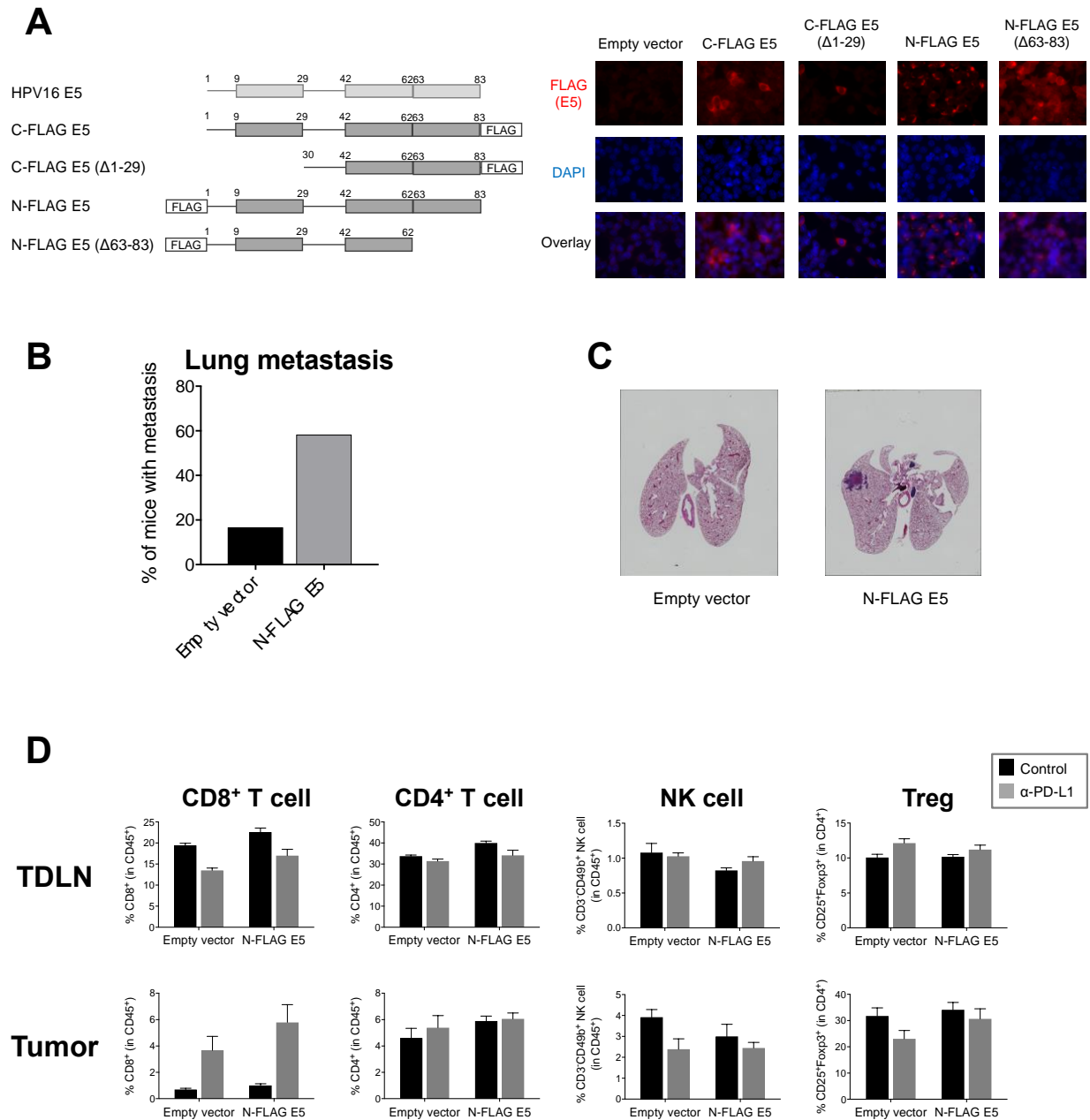


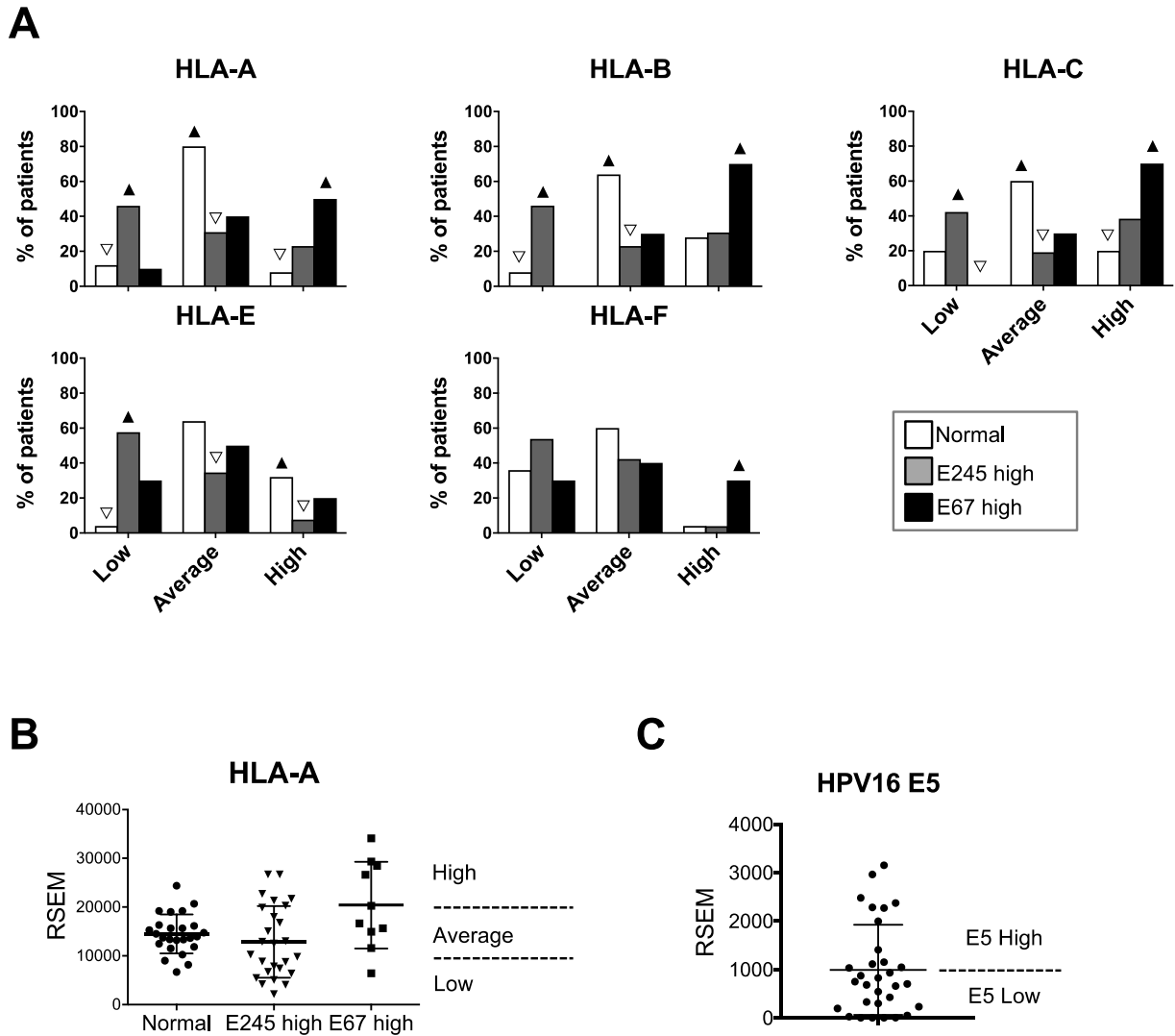
Supplementary Materials:



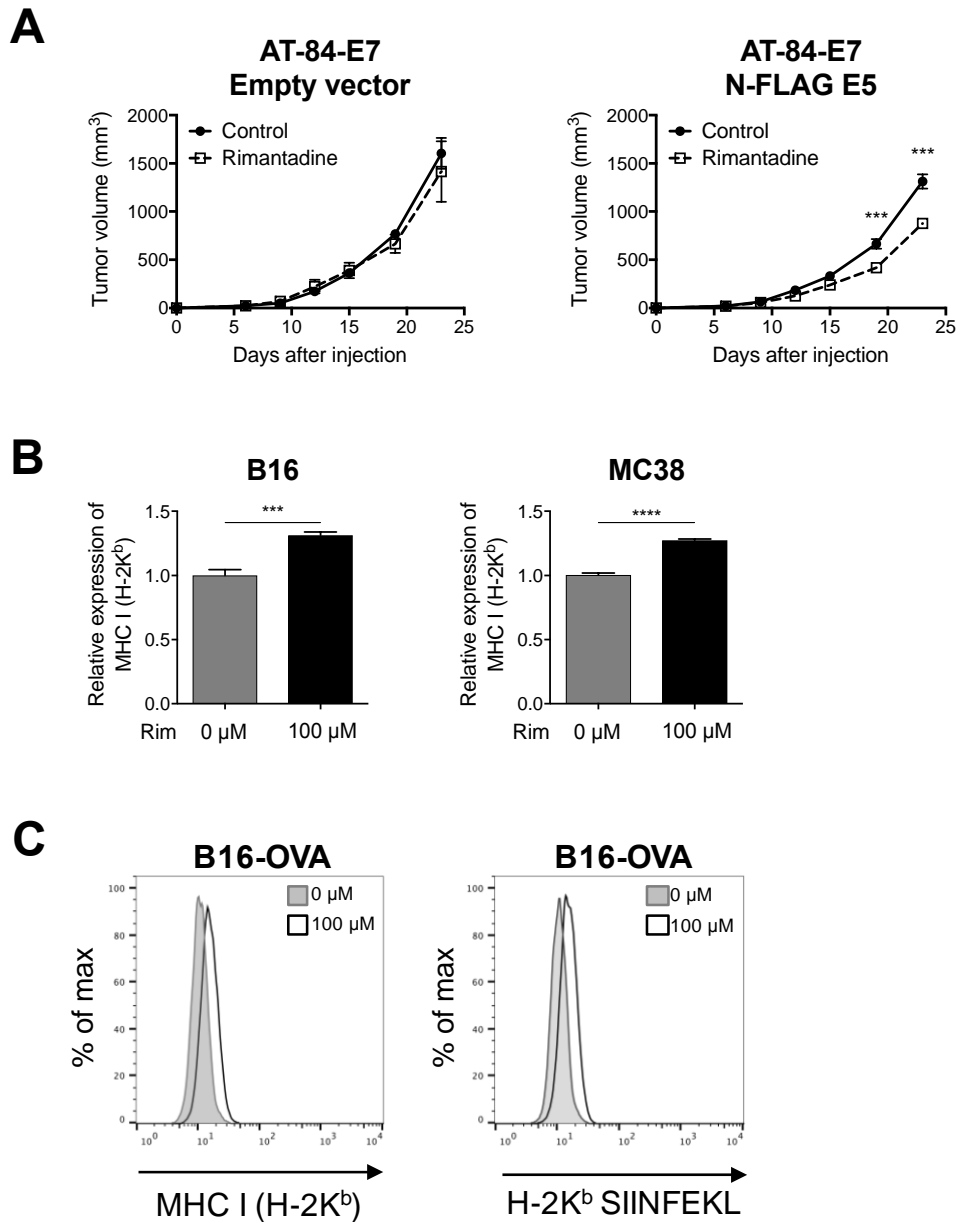
Supplementary Figure 1: Radiation combined with anti-PD-L1 immunotherapy activates CD8⁺ T cells, but decreases regulatory T cell population in a head and neck cancer model. **A)** Representative dot plots of IFN- γ ⁺ cells in CD8⁺ T cells in the TDLN from an AT-84-E7 orthotopic model. **B)** Representative dot plots of CD25⁺Foxp3⁺ regulatory T cells within CD4⁺ T cells from the TDLN in an AT-84-E7 flank model. **C)** Memory subsets of CD8⁺ T cells in TIL from AT-84-E7-bearing mice. **D)** Percentage of CD25⁺Foxp3⁺ regulatory T cells within CD4⁺ T cells from TIL in an AT-84-E7 flank model. **E)** mRNA expression of chemokines in irradiated- and nonirradiated- LN from HNSCC patient was analyzed by RT-qPCR. Data are shown as mean \pm S.E.M. Abbreviations: TDLN, tumor-draining lymph node; TIL, tumor-infiltrating lymphocyte



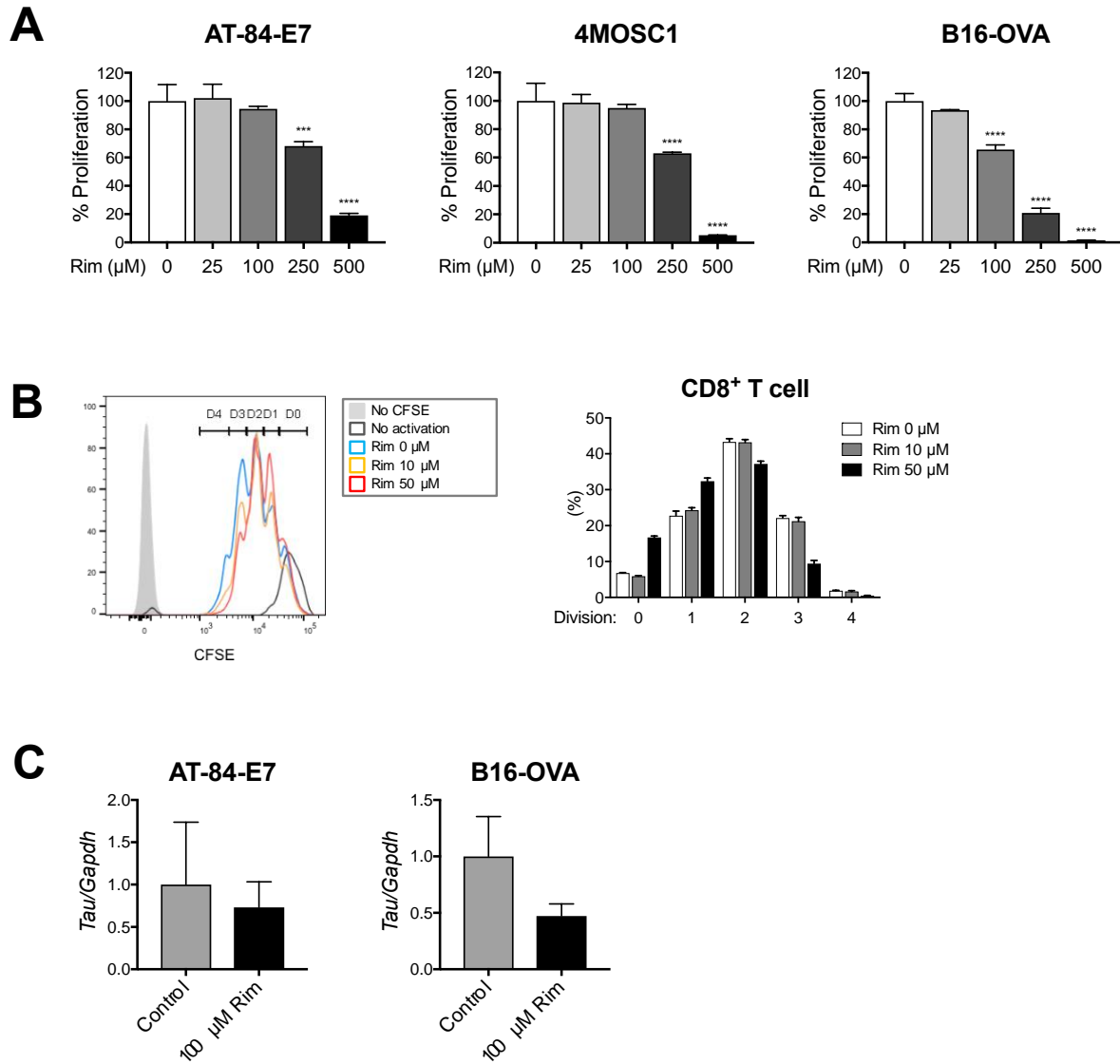
Supplementary figure 2: N-FLAG E5 localized in Golgi apparatus and promoted lung metastasis. A) (left) HPV16 E5 construct schemes. (right) Immunofluorescence of E5 (red) and nuclei (blue) in transiently transfected HEK293T. **B)** Percentage of the mice with lung metastasis among AT-84-E7-bearing mice on Day 28 after tumor inoculation. **C)** Representative images of lung metastasis stained with H&E. **D)** Flow cytometric analysis of various immune cell population in TDLN and tumor. Data are shown as mean \pm S.E.M. Statistics were done using an unpaired *t*-test.



Supplementary figure 3: Patients with high expression of HPV16 E5 have low HLA expression **A, B**) mRNA expression of different types of HLAs. Patients were assigned to 3 groups (high, average, and low) based on each HLA expression. Graph **B**) shows HLA-A as an example. Chi-square test (X^2 and p -value) and residual analysis (\blacktriangle : significantly high, ∇ : significantly low, $P < 0.05$). **C**) mRNA expression of HPV16 E5. Patients were divided into 2 groups (high- and low- expression) based on expression relative to the median.



Supplementary figure 4: Rimantadine enhances MHC expression and antigen-presentation on tumor cells. **A)** 5×10^5 AT-84-E7 cells expressing empty vector or FLAG-tagged E5 were subcutaneously injected and treated with rimantadine for one week. $n = 6$ in each group. **B)** MHC I expression was analyzed by flow cytometry 48 hours after rimantadine treatment. **C)** Expression of MHC I and antigen presentation (H-2K^b/SIINFEKL) 24 hours after rimantadine treatment.



Supplementary Figure 5: Rimantadine inhibits cell proliferation in head and neck cancer cell lines and downregulates microtubule-associated molecules. **A)** Cell proliferation (MTT) was analyzed 48 hours following treatment with rimantadine. **B)** T-cell proliferation (CFSE) was analyzed 72 hours following treatment with rimantadine. **C)** *Tau* mRNA expression was analyzed 24 hours following treatment with rimantadine. Data are shown as mean \pm S.E.M. Statistics were done using an unpaired *t*-test or one-way ANOVA.

Supplementary Table 1: Clinical data of HNSCC Johns Hopkins University cohort

	Normal (n = 25)	E245 high (n = 25)	E67 high (n = 10)
Age			
Median	27	56	51
Minimum	18	44	37
Maximum	51	75	65
Sex			
Male	10 (40%)	22 (88%)	9 (90%)
Female	15 (60%)	3 (12%)	1 (10%)
Race			
White	14 (56%)	24 (96%)	10 (100%)
Black	9 (36%)	0 (0%)	0 (0%)
Asian	0 (0%)	1 (4%)	0 (0%)
Other	2 (8%)	0 (0%)	0 (0%)
Smoking			
Never	19 (76%)	11 (44%)	2 (20%)
Current	4 (16%)	7 (28%)	2 (20%)
Former	2 (8%)	7 (28%)	6 (60%)
Integration			
Yes		2 (8%)	10 (100%)
Subtype			
IMS		13 (52%)	3 (30%)
BA		7 (28%)	3 (30%)
CL		5 (20%)	4 (40%)
T stage			
T0		2 (8%)	0 (0%)
T1		9 (36%)	4 (40%)
T2		11 (44%)	4 (40%)
T3		3 (12%)	1 (10%)
T4		0 (0%)	1 (10%)
N stage			
0		0 (0%)	1 (10%)
1		19 (76%)	8 (80%)
2		4 (16%)	1 (10%)
3		2 (8%)	0 (0%)
Advanced N stage (2 and 3)		6 (24%)	1 (10%)
M stage			
0		25 (100%)	10 (100%)
Stage			
1		18 (72%)	7 (70%)
2		5 (20%)	2 (20%)
3		2 (8%)	1 (10%)
4		0 (0%)	0 (0%)
Overall survival			
Alive		20 (80%)	7 (70%)
Dead		5 (20%)	3 (30%)
Recurrence			
Yes		2 (8%)	0 (0%)

Supplementary Table 2: HPV status and HLA mRNA expression level

	Normal (n = 25)	E245 high (n = 26)	E67 high (n = 10)	χ^2	P-value
HLA-A					
Low (<10000)	3 (12%) ▽	12 (46.2%) ▲	1 (10%)	19.090	0.0008 ***
Average (10000-20000)	20 (80%) ▲	8 (30.8%) ▽	4 (40%)		
High (20000<)	2 (8%) ▽	6 (23.1%)	5 (50%) ▲		
HLA-B					
Low (<15000)	2 (8%) ▽	12 (46.2%) ▲	0 (0%)	20.235	0.0004 ***
Average (15000-30000)	16 (64%) ▲	6 (23.1%) ▽	3 (30%)		
High (30000<)	7 (28%)	8 (30.8%)	7 (70%) ▲		
HLA-C					
Low (<6000)	5 (20%)	11 (42.3%) ▲	0 (0%) ▽	16.385	0.0025 **
Average (6000-13000)	15 (60%) ▲	5 (19.2%) ▽	3 (30%)		
High (13000<)	5 (20%) ▽	10 (38.5%)	7 (70%) ▲		
HLA-E					
Low (<8000)	1 (4%) ▽	15 (57.7%) ▲	3 (30%)	17.869	0.0013 **
Average (8000-15000)	16 (64%)	9 (34.6%) ▽	5 (50%)		
High (15000<)	8 (32%) ▲	2 (7.7%) ▽	2 (20%)		
HLA-F					
Low (<2000)	9 (36%)	14 (53.8%)	3 (30%)	9.353	0.0529
Average (2000-4000)	15 (60%)	11 (42.3%)	4 (40%)		
High (4000<)	1 (4%)	1 (3.8%)	3 (30%) ▲		

Patients were assigned to 3 groups based on the mRNA expression level (low, average, and high). Table shows the results of Chi-square test (χ^2 and p -value) and residual analysis (▲: significantly high, ▽: significantly low, $P < 0.05$).