

Table SI. Patient characteristics (n=45).

Variable	Value
Median age, years (range)	67 (35-84)
Sex, n (%)	
Male	29 (64)
Female	16 (36)
ECOG PS, n (%)	
0	34 (76)
1	6 (13)
2	1 (2)
3	4 (9)
Primary site, n (%)	
Tongue	24 (53)
Buccal mucosa	4 (9)
Oral floor	4 (9)
Upper gingiva	6 (13)
Lower gingiva	5 (11)
Upper lip	1 (2)
Mandible	1 (2)
Stage, n (%)	
I	4 (9)
II	13 (29)
III	4 (9)

IV	24 (53)
ICI, n (%)	
Nivolumab	23 (51)
Pembrolizumab	22 (49)
Administration line, n (%)	
1st	25 (56)
2nd	19 (42)
3rd	1 (2)
Initial treatment: Operation, n (%)	
Yes	42 (93)
No	3 (7)
Initial treatment: Radiotherapy, n (%)	
Yes	39 (87)
No	6 (13)
Target lesion, n (%)	
Local	12 (27)
Regional LN	5 (11)
Distal metastasis	21 (47)
Local, regional LN	1 (2)
Local, distant metastasis	3 (7)
Regional LN, distant metastasis	2 (4)
Local, regional LN, distant metastasis	1 (2)
CPS, n (%)	

<1%	4 (9)
1-20%	4 (9)
≥20%	29 (64)
Administration method, n (%)	
Monotherapy	33 (73)
Chemotherapy combination	8 (18)
Chemotherapy combination → Mono	4 (9)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; ICI, immune checkpoint inhibitor; LN, lymph node; CPS, Combined Positive Score.

Table SII. Response to nivolumab and immune-related adverse events. Clinical outcomes of patients treated with ICI (n=45).

Variable	Value	%
Median number of administration (range)	5 (1-68)	
Response		
CR	4	9
PR	6	13
SD	5	11
PD	30	67
ORR (CR + PR)	10	22
DCR (CR + PR + SD)	15	33
irAE		
No	32	71
Yes	13	29
Thyroid dysfunction (hyperthyroidism/hypothyroidism)	1/3	9
Interstitial pneumonia (Grade 1/Grade 3)	2/1	7
Colitis (Grade 2/Grade 3)	1/1	4
Dermatologic disorders	1	2
Interstitial nephritis (Grade 3)	1	2
Hypopituitarism	1	2

Liver dysfunction (Grade 3)	1	2
Atrial fibrillation	1	2
Acute kidney failure	1	2

CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease;
ORR, overall response rate; DCR, disease control rate; irAE, immune-related adverse
events.

Table SIII. AUC data.

AUC	Pre	Post
NLR	0.53802	0.76959
LMR	0.47350	0.68779
PNI	0.59217	0.69585
PLR	0.50691	0.64747
CAR	0.39516	0.73618
Eosinophil	0.55876	0.51382
Lymphocytes	0.58641	0.69935

AUC, area under the curve; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PNI, prognostic nutritional index; PLR, platelet-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio.

Table SIV. Univariate and multivariate analysis of prognosis factors for PFS.

Variable	Number	Univariate			Multivariate		
		HR	95% CI	P-value	HR	95% CI	P-value
Age, years							
<65	20	Ref.					
≥65	25	1.34	0.67-2.69	0.406			
Sex							
Male	29	1.26	0.61-2.62	0.523	3.86	1.32-11.31	0.0138 ^a
Female	16	Ref.					
ECOG PS							
0	34	Ref.					
≥1	11	4.64	2.01-10.72	0.0003 ^a			
ICI							
Nivolumab	23	1.90	0.95-3.80	0.069	11.75	2.68-51.49	0.0011 ^a
Pembrolizumab	22	Ref.					
irAE							
Positive	13	Ref.					
Negative	32	1.40	0.65-3.03	0.378			
ICI combination							
Monotherapy	33	Ref.					
With	12	2.13	0.82-5.52	0.092			

chemotherapy							
Radiation							
Previously	39	Ref.					
No	6	2.57	1.03-6.44	0.043 ^a			
BMI, kg/m ²							
<18.37	20	1.57	0.79-3.14	0.199			
≥18.37	25	Ref.					
CPS							
<20	8	1.41	0.55-3.59	0.488			
≥20	29	Ref.					
DCR							
CR/PR/SD	15	Ref.					
PD	40	5.54	2.15-14.27	0.0004 ^a	9.15	2.38-35.14	0.0013 ^a
Primary site							
Tongue	24	Ref.					
Otherwise	21	1.75	0.88-3.50	0.114	4.87	1.51-15.72	0.0081 ^a

^aIndicates a significant difference among groups with P<0.05. PFS, progression-free survival; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ICI, immune checkpoint inhibitor; irAE, immune-related adverse events; BMI, body mass index; CPS, Combined Positive Score; DCR, disease control rate; HR, hazard ratio; CI, confidence interval; Ref, Reference.

Table SV. Univariate and multivariate analysis of pre- and post-treatment factors for PFS.

A, Pre-treatment factors							
Variable	Number	Univariate			Multivariate		
		HR	95% CI	P-value	HR	95% CI	P-value
Age, years							
<65	20	Ref.					
≥65	25	1.34	0.67-2.69	0.406			
Sex							
Male	29	1.26	0.61-2.62	0.523	4.74	1.59-14.15	0.0052 ^a
Female	16	Ref.					
ECOG PS							
0	34	Ref.					
≥1	11	4.64	2.01-10.72	0.0003 ^a			
CPS							
<20	8	1.41	0.55-3.59	0.488			
≥20	29	Ref.					
ICI combination							
Mono	33	Ref.					
With chemotherapy	12	2.13	0.82-5.52	0.092			
Radiation							
Previously	39	Ref.					

No	6	2.57	1.03-6.44	0.043 ^a			
BMI, kg/ m ²							
<18.37	20	1.57	0.79-3.14	0.199			
≥18.37	25	Ref.					
Pre-NLR							
<4.7	16	Ref.					
≥4.7	29	1.16	0.63-2.15	0.632			
Pre-LMR							
<1.29	32	Ref.					
≥1.29	13	1.62	0.82-3.20	0.152			
Pre-PNI							
<43.75	30	1.12	0.59-2.12	0.726			
≥43.75	15	Ref.					
Pre-PLR							
<453.5	31	1.86	0.96-3.61	0.057			
≥453.5	14	Ref.					
Pre-CAR							
<6.35	43	Ref.					
≥6.35	2	2.10	0.50-8.88	0.362			
Pre- eosinophils							
<120	18	1.06	0.56-2.00	0.861			

≥120	27	Ref.					
Pre-lymphocytes							
<670	29	Ref.					
≥670	16	1.14	0.54-2.40	0.733			
B, Post-treatment factors							
		Univariate			Multivariate		
Variable	Number	HR	95% CI	P-value	HR	95% CI	P-value
irAE							
Positive	13	Ref.					
Negative	32	1.40	0.65-3.03	0.378			
Post-NLR							
<7.17	22	Ref.					
≥7.17	23	2.21	1.14-4.29	0.014 ^a	3.80	1.11-13.02	0.0339 ^a
Post-LMR							
<1.23	15	1.11	0.53-2.35	0.781			
≥1.23	30	Ref.			4.02	1.14-14.18	0.0304 ^a
Post-PNI							
<36.6	16	3.25	1.61-6.55	0.0015 ^a	2.96	1.08-8.06	0.0342 ^a
≥36.6	29	Ref.					
Post-PLR							
<221.1	13	Ref.					

≥221.1	32	1.43	0.66-3.10	0.352			
Post-CAR							
<0.44	22	Ref.					
≥0.44	23	2.93	1.44-5.96	0.0029 ^a			
Post-eosinophil							
<260	32	1.33	0.61-2.88	0.463			
≥260	13	Ref.					
Post-lymphocytes							
<770	21	Ref.					
≥770	25	1.05	0.52-2.11	0.902			
Post-mGPS							
0	13	Ref.					
1	33	2.01	0.90-4.50	0.088			

^aIndicates a significant difference among groups with P<0.05. PFS, progression-free survival; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CPS, Combined Positive Score; ICI, immune checkpoint inhibitor; BMI, body mass index; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PNI, prognostic nutritional index; PLR, platelet-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; HR, hazard ratio; CI, confidence interval; Ref, reference.

Table SVI. Univariate analysis of prognostic factors for the DCR.

Variable	Response	Value (%)	P-value
Age, years			0.071
<65	CR/PR/SD	9 (20)	
	PD	11 (24)	
≥65	CR/PR/SD	5 (11)	
	PD	20 (44)	
Sex			0.988
Male	CR/PR/SD	9 (20)	
	PD	20 (44)	
Female	CR/PR/SD	5 (11)	
	PD	11 (24)	
ECOG PS			0.0018 ^a
0	CR/PR/SD	14 (31)	
	PD	20 (45)	
≥1	CR/PR/SD	0 (0)	
	PD	11 (24)	
CPS			0.007 ^a
<20	CR/PR/SD	1 (2)	
	PD	7 (16)	
≥20	CR/PR/SD	13 (29)	
	PD	16 (36)	
BMI, kg/m ²			0.032 ^a

<18.37	CR/PR/SD	3 (7)	
	PD	17 (38)	
≥18.37	CR/PR/SD	11 (24)	
	PD	14 (31)	
Primary site			0.319
Tongue	CR/PR/SD	9 (20)	
	PD	15 (33)	
Otherwise	CR/PR/SD	5 (11)	
	PD	16 (36)	
irAE			0.502
Positive	CR/PR/SD	5 (11)	
	PD	8 (18)	
Negative	CR/PR/SD	9 (20)	
	PD	23 (51)	
ICI			0.364
Mono	CR/PR/SD	9 (20)	
	PD	24 (53)	
Combination	CR/PR/SD	5 (11)	
	PD	7 (16)	
Radiation			0.027 ^a
Previously	CR/PR/SD	14 (31)	
	PD	25 (56)	
No	CR/PR/SD	0 (0)	

	PD	6 (13)	
Number of ICI administration			0.078
<3	CR/PR/SD	1 (2)	
	PD	9 (20)	
≥3	CR/PR/SD	13 (29)	
	PD	22 (49)	
Recurrent/metastasis status			0.730
Locoregional	CR/PR/SD	8 (18)	
	PD	16 (36)	
Distant	CR/PR/SD	6 (13)	
	PD	16 (33)	
Pre-NLR			0.178
<4.7	CR/PR/SD	7 (16)	
	PD	9 (20)	
≥4.7	CR/PR/SD	7 (16)	
	PD	22 (49)	
Pre-LMR			0.172
<1.29	CR/PR/SD	6 (13)	
	PD	7 (16)	
≥1.29	CR/PR/SD	8 (18)	
	PD	24 (53)	

Pre-PNI			0.259
<43.75	CR/PR/SD	8 (18)	
	PD	23 (51)	
≥43.75	CR/PR/SD	6 (13)	
	PD	8 (18)	
Pre-PLR			0.259
<453.5	CR/PR/SD	8 (18)	
	PD	23 (51)	
≥453.5	CR/PR/SD	6 (13)	
	PD	8 (18)	
Pre-CAR			0.570
<6.35	CR/PR/SD	13 (29)	
	PD	30 (67)	
≥6.35	CR/PR/SD	1 (2)	
	PD	1 (2)	
Pre-eosinophils			0.117
<120	CR/PR/SD	8 (18)	
	PD	10 (22)	
≥120	CR/PR/SD	6 (13)	
	PD	21 (47)	
Pre-lymphocytes			0.244
<670	CR/PR/SD	3 (7)	
	PD	12 (27)	

≥670	CR/PR/SD	11 (24)	
	PD	19 (42)	
Post-NLR			0.0006 ^a
<7.17	CR/PR/SD	12 (27)	
	PD	10 (22)	
≥7.17	CR/PR/SD	2 (4)	
	PD	21 (47)	
Post-LMR			0.0065 ^a
<1.23	CR/PR/SD	1 (2)	
	PD	14 (31)	
≥1.23	CR/PR/SD	13 (29)	
	PD	17 (38)	
Post-PNI			0.0358 ^a
<36.6	CR/PR/SD	2 (4)	
	PD	14 (31)	
≥36.6	CR/PR/SD	12 (27)	
	PD	17 (38)	
Post-PLR			0.0396 ^a
<221.1	CR/PR/SD	7 (16)	
	PD	6 (13)	
≥221.1	CR/PR/SD	7 (16)	
	PD	25 (56)	
Post-CAR			0.0062 ^a

<0.44	CR/PR/SD	11 (24)	
	PD	11 (24)	
≥0.44	CR/PR/SD	3 (7)	
	PD	20 (44)	
Post-eosinophils			0.502
<260	CR/PR/SD	9 (20)	
	PD	23 (51)	
≥260	CR/PR/SD	5 (11)	
	PD	8 (18)	
Post-lymphocytes			0.0321 ^a
<770	CR/PR/SD	3	
	PD	17	
≥770	CR/PR/SD	11 (24)	
	PD	14 (31)	

^a Indicates a significant difference among groups with $P < 0.05$. DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CPS, Combined Positive Score; BMI, body mass index; irAE, immune-related adverse events; ICI, immune checkpoint inhibitor; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PNI, prognostic nutritional index; PLR, platelet-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.