

Table SI. Relationship between clinicopathological characteristics and pre-treatment miRNA levels without OAA1 enrichment.

Clinicopathologic al characteristic	miR-320a			miR-320b			miR-3613-5p		
	Low (n=23)	High (n=25)	P-value	Low (n=13)	High (n=35)	P-value	Low (n=21)	High (n=27)	P-value
Mean \pm SD age, years	67.7 \pm 8.35	63.68 \pm 10.8 6	0.16	66.4 \pm 7.88	65.31 \pm 10.5 7	0.742	65.95 \pm 10.4 9	65.31 \pm 9.52	0.854
Sex ^a									
Male	18	20	1.0	11	27	0.706	18	20	0.478
Female	5	5		2	8		3	7	
Smoking status ^a									
Smoker	3	3	1.0	13	29	0.171	19	23	0.683
Nonsmoker	20	22		0	6		2	4	
Levels of tumor markers ^a									
Low	9	11	1.0	5	15	0.749	10	10	0.371
High	12	14		8	18		9	17	
Unknown	2	0		0	2		2	0	

Pathology ^a									
ADC	16	17	1.0	9	24	1.0	14	19	1.0
SQC	7	8		4	11		7	8	
Recurrent disease ^b									
Yes	9	15	0.149	5	19	0.33	10	14	0.771
No	14	10		8	16		11	13	
Driver mutations ^a									
EGFR	0	3	0.339	0	3	0.836	2	1	0.534
ALK	1	0		0	1		0	1	
Wild-type	15	14		9	20		11	18	
Unknown	7	8		4	11		8	7	
PD-L1 status ^a									
Negative	7	4	0.671	4	7	1.0	6	5	1.0
Positive	13	4		7	10		10	7	
Unknown	3	17		2	17		5	15	

CD8 expression ^a									
Negative	5	1	0.640	2	4	1.0	3	3	1.0
Positive	15	7		9	13		13	9	
Unknown	3	17		2	18		5	15	
Mean \pm SD number of previous regimens	2.39 \pm 1.87	2.20 \pm 1.41	0.69	2.15 \pm 1.91	2.34 \pm 1.55	0.73	2.05 \pm 1.86	2.48 \pm 1.45	0.368
IrAE ^a									
Absent	6	4	0.487	4	6	0.425	5	5	0.729
Present	17	21		9	29		16	22	
Clinical responses to nivolumab ^a									
PR	9	12	0.162	7	3	0.002 ^c	9	1	0.001 ^c
SD + PD	16	22		6	32		12	26	

Reasons for treatment discontinuation ^a									
Disease progression	16	18	0.183	8	26	0.173	15	19	0.605
IrAE	3	2		2	3		2	3	
PS down	1	5		1	5		2	4	
Death by AMI	1	0		0	1		0	1	
Treatment continuation	2	0		2	0		2	0	

^aFisher's exact test. ^b χ^2 test. ^cP<0.05. ADC, adenocarcinoma; ALK, anaplastic lymphoma kinase; AMI, acute myocardial infarction; EGFR, epidermal growth factor; irAE, immune-related adverse events; OAA1, *Oscillatoria agardhii* agglutinin 1; PD-L1, programmed death ligand 1; PR, partial response; PS, performance status; SD + PD, stable or progressive disease; SQC, squamous cell carcinoma.

Table SII. Relationship between clinicopathological characteristics, pre-treatment levels of miRNAs, and OAA1 enrichment.

Clinicopathological characteristic	OAA1 captured miR-320a			OAA1 captured miR-320b			OAA1 captured miR-3613-5p		
	Low (n=17)	High (n=31)	P-value	Low (n=10)	High (n=38)	P-value	Low (n=16)	High (n=32)	P-value
Mean \pm SD age, years	66.71 \pm 7.166	65.00 \pm 11.11	0.672	66.9 \pm 8.66	65.26 \pm 10.22	0.645	66.31 \pm 9.96	65.25 \pm 9.93	0.73
Sex ^a									
Male	15	23	0.459	9	29	0.664	12	26	0.712
Female	2	8		1	9		4	6	
Smoking status ^a									
Smoker	17	25	0.077	10	32	0.320	14	28	1
Nonsmoker	0	6		0	6		2	4	
Levels of tumor									

markers ^a									
Low	9	11	0.369	6	14	0.292	6	14	1.0
High	8	18		4	22		8	18	
Unknown	0	2		0	2		2	0	
Pathology ^a									
ADC	12	21	1.0	8	25	0.472	11	22	1
SQC	5	10		2	13		5	10	
Recurrent disease ^b									
Yes	8	16	0.763	5	19	1	6	18	0.221
No	9	15		5	19		10	14	
Driver mutations ^a									
EGFR	0	3	0.675	0	1	1	0	3	0.116
ALK	0	1		0	3		0	1	
Wild-type	11	18		7	22		10	9	
Unknown	6	9		3	12		6	19	

PD-L1 status ^a									
Negative	7	4	0.246	3	8	1	3	8	0.102
Positive	7	10		6	11		10	7	
Unknown	3	17		1	19		3	17	
CD8 expression ^a									
Negative	4	2	0.648	1	5	0.630	1	5	0.173
Positive	10	12		8	14		12	10	
Unknown	3	17		1	19		3	17	
Mean ± SD number of previous regimens	2.18±1.776	2.35±1.58	0.499	2.10±2.18	2.34±1.49	0.682	2.00±1.93	2.44±1.48	0.388
IrAE ^a									
Absent	5	5	0.295	3	7	0.414	5	5	0.267
Present	12	26		7	31		11	27	
Clinical responses to nivolumab ^a									

PR	8	2	0.002 ^c	7	3	<0.001 ^c	9	1	<0.001 ^c
SD + PD	9	29		3	35		7	31	
Reasons for treatment discontinuation ^a									
Disease progression	12	22	0.314	5	29	0.045 ^c	10	24	0.125
IrAE	2	3		2	3		3	2	
PS down	1	5		1	5		1	5	
Death by AMI	0	1		0	1		0	1	
Treatment continuation	2	0		2	0		2	0	

^aFisher's exact test. ^b χ^2 test. ^cP<0.05. ADC, adenocarcinoma; ALK, anaplastic lymphoma kinase; AMI, acute myocardial infarction; EGFR, epidermal growth factor; irAE, immune-related adverse events; OAA1, *Oscillatoria agardhii* agglutinin 1; PD-L1, programmed death ligand 1; PR, partial response; PS, performance status; SD + PD, stable or progressive disease; SQC, squamous cell carcinoma.

Table SIII. Multivariate Cox regression analysis of clinicopathological factors and circulating miRNA levels without OAA1 enrichment.

Clinicopathological characteristic	Hazard ratio (95% CI)	P-value
CD8 expression		
Negative	1	0.008 ^a
Positive	0.149 (0.037-0.603)	
Levels of miR-320a		
Low	1	0.211
High	2.468 (0.599-10.17)	
Levels of miR-320b		
Low	1	0.024 ^a
High	5.505 (1.247-24.31)	
Levels of miR-3613-5p		
Low	1	0.048 ^a

High	3.152 (1.009-9.847)	
------	---------------------	--

^aP<0.05. CI, confidence interval; miR, microRNA; OAA1, *Oscillatoria agardhii* agglutinin 1.

¥

Table SIV. Multivariate Cox regression analysis of clinicopathological factors and circulating miRNA levels with OAA1 enrichment.

Clinicopathological characteristic	Hazard ratio (95% CI)	P-value
CD8 expression		
Negative	1	0.301
Positive	0.377 (0.059-2.395)	
Levels of OAA1 captured miR-320a		
Low	1	0.684
High	1.518 (0.204-11.29)	
Levels of OAA1 captured miR-320b		
Low	1	0.114
High	4.924 (0.682-33.55)	

Levels of OAA1 captured miR-3613-5p		
Low	1	0.010 ^a
High	7.462 (1.610-34.63)	

^aP<0.05. CI, confidence interval; miR, microRNA; OAA1, *Oscillatoria agardhii* agglutinin 1.