## **Supplementary Materials**

## Exploring YAP1-related TIME in SCLC: implications for survival and treatment response to immuno-chemotherapy

## Yu-Qing Chen<sup>1,2,3,#</sup>, Jia-Xiong Tan<sup>1,2,3,#</sup>, Ling-Ling Gao<sup>4,#</sup>, Jia-Xing Yang<sup>1,2,3</sup>, Jie Huang<sup>5</sup>, Jin-Ji Yang<sup>5</sup>, Qiang Zhao<sup>1,2,3,6</sup>

<sup>1</sup>Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin 300060, China.

<sup>2</sup>Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China.

<sup>3</sup>Key Laboratory of Cancer Prevention and Therapy, Tianjin 300060, China.

<sup>4</sup>Beihang University, Beijing 100191, China.

<sup>5</sup>Guangdong Lung Cancer Institute, Guangdong Provincial Key Laboratory of Translational Medicine in Lung Cancer, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou 510080, Guangdong, China. <sup>6</sup>Department of Pediatric Oncology, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin 300060, China.

<sup>#</sup>Authors contributed equally.

**Correspondence to:** Dr. Qiang Zhao, Department of Pediatric Oncology, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Ti Yuan north, Huanhu west road, Tianjin 300060, China. E-mail: zhaoqiang@tjmuch.com; Dr. Jin-Ji Yang, Guangdong Lung Cancer Institute, Guangdong Provincial Key Laboratory of Translational Medicine in Lung Cancer, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, 106 Zhongshan 2nd Road, Guangzhou 510080, Guangdong, China. E-mail: yangjinji@gdph.org.cn



Time

Time **Supplementary Figure 1.** K=M curves for survival analysis.



**Supplementary Figure 2.** Potential prognostic value of YAP1 in ES-SCLC. The linear regression fiting curve calculated by speamman correlation betwen 0S and cell population, cell density, cell density in tumor stroma and cell population in tumor parenchyma of YAP1 positive cells respectively. ES-SCLC: Extensive-stage small cell lung cancer; OS: overall survival.

Patient	Gende	Ag	Smoke	<b>Confirmed Diagnosis</b>	Dathalagy	Mix	NSE	Ki67	Line of	BO	PFS	OS
Number	r	e	(pack*years)	Time	Pathology	Туре	(ng/ml)	(%)	ECT	R	(d)	(d)
1	F	66	0	2021/6/3	SCLC	NA	112.6	90	1st	PR	152	361
2	М	55	30	2020/5/26	SCLC	NA	18.47	90	2nd	SD	135	271
3	М	72	0	2020/3/18	SCLC	NA	115.1	90	1st	PR	108	515
4	М	62	100	2020/8/14	SCLC	NA	41.65	80	1st	SD	132	154
5	М	68	80	2019/3/22	SCLC	NA	40.93	90	1st	SD	284	616
6	М	66	40	2019/3/18	SCLC	NA	155	60	1st	PR	212	298
7	М	62	20	2021/2/5	SCLC Mix	LUSC	>370	90	1st	SD	103	130
8	М	70	0	2021/7/8	SCLC	NA	90.09	80	1st	SD	144	191
9	М	54	45	2022/4/12	SCLC	NA	128.6	80	1st	PD	58	297
10	М	72	80	2022/1/12	SCLC	NA	63.7	80	1st	PR	227	810+
11	М	61	17.5	2021/12/30	SCLC	NA	62.54	90	1st	PR	224	804+
12	М	59	30	2022/1/4	SCLC	NA	25.86	95	1st	PR	152	407
13	М	75	50	2022/1/7	SCLC	NA	16.13	80	1st	PR	52	479
14	М	64	80	2021/2/2	SCLC	NA	21.4	90	1st	SD	453	985
15	F	71	0	2021/12/31	SCLC	NA	49.66	80	1 st	SD	133	409

Supplementary Table 1. Clinical and pathological characteristics of ES-SCLC patients received ECT regimen in this study

ES-SCLC, extensive-stage small cell lung cancer; ECT, atezolizumab plus etoposide/ carboplatin.

			Responder group		non-R	non-Responder group		
		-	mean	95% CI	mean	96% CI	-	
		total	0.1140	0.0359-0.2223	0.1152	0.0456-0.1907	0.985	
	cell population	parenchyma	0.0356	0.0073-0.0672	0.0503	0.0180-0.0989	0.623	
CD4 manitizer anlla		stroma	0.1075	0.0584-0.1617	0.1662	0.0623-0.2712	0.366	
CD4 positive cells	cell density	total	0.0008	0.0003-0.0013	0.0012	0.0004-0.0022	0.485	
		parenchyma	0.0006	0.0001-0.0011	0.0007	0.0002-0.0015	0.704	
		stroma	0.0010	0.0004-0.0017	0.0016	0.0008-0.0026	0.351	
	cell population	total	0.0119	0.0062-0.0183	0.0162	0.0033-0.0329	0.632	
		parenchyma	0.0046	0.0012-0.0092	0.0055	0.0006-0.0134	0.860	
		stroma	0.0249	0.0124-0.0402	0.0240	0.0124-0.0402	0.951	
roxps positive cens		total	0.0001	0.0001-0.0002	0.0002	0-0.0003	0.778	
	cell density	parenchyma	0.0001	0-0.0001	0.0001	0-0.0003	0.850	
		stroma	0.0002	0.0001-0.0004	0.0002	0.0001-0.0005	0.861	
	cell population	total	0.0485	0.0235-0.0813	0.0701	0.0141-0.1448	0.617	
		parenchyma	0.0196	0.0117-0.0332	0.0308	0.0031-0.0784	0.672	
CD9		stroma	0.0728	0.0403-0.1082	0.0989	0.0237-0.1964	0.597	
CD8 positive cells		total	0.0005	0.0003-0.0007	0.0007	0.0001-0.0017	0.608	
	cell density	parenchyma	0.0003	0.0001-0.0002	0.0005	0-0.0013	0.664	
		stroma	0.0006	0.0004-0.0009	0.0009	0.0002-0.0019	0.618	
	ve cells cell population	total	0.3725	0.1206-0.6407	0.4700	0.3779-0.5482	0.524	
CD56 positive cells		parenchyma	0.6412	0.3818-0.8778	0.7799	0.6899-0.8620	0.373	
		stroma	0.1442	0.0401-0.2987	0.2216	0.1275-0.3269	0.382	

## Supplementary Table 2. Differences of different types of cells between the responder group and non-responder group

		total	0.0057	0.0029-0.0085	0.0042	0.0032-0.0052	0.308
	cell density	parenchyma	0.0101	0.0053-0.0143	0.0105	0.0092-0.0120	0.853
		stroma	0.0011	0.0004-0.0022	0.0045	0.0010-0.0116	0.390
	cell population	total	0.0351	0.0246-0.0446	0.1178	0.0680-0.1640	0.014
		parenchyma	0.0189	0.0083-0.0331	0.0737	0.0179-0.1485	0.159
VAD1 magitizza aglia		stroma	0.0182	0.0004-0.0431	0.1296	0.0348-0.2296	0.064
Y AP1 positive cells	cell density	total	0.0004	0.0003-0.0006	0.0013	0.0007-0.0019	0.028
		parenchyma	0.0003	0.0001-0.0005	0.0010	0.0004-0.0016	0.338
		stroma	0.0006	0.0004-0.0008	0.0075	0.0005-0.0250	0.112