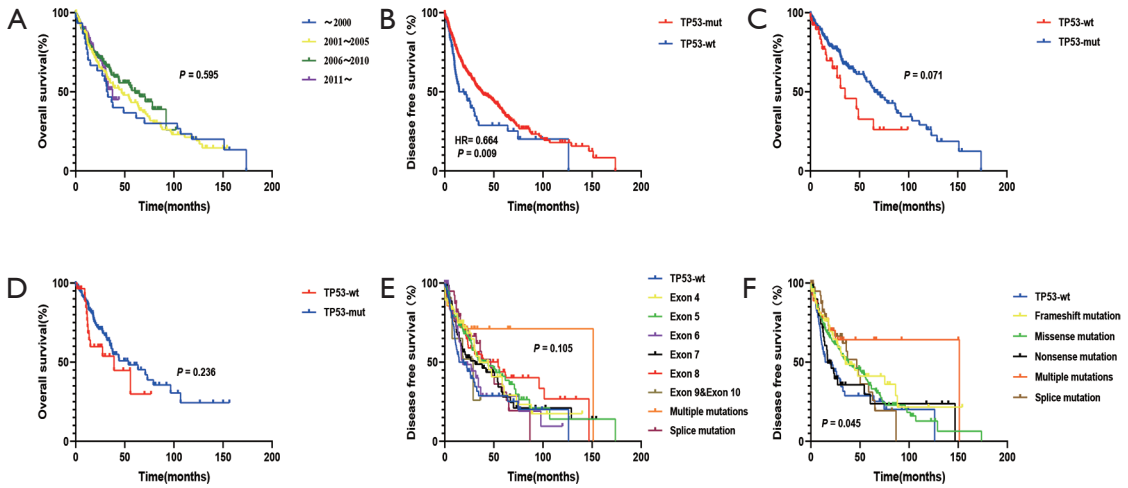

Figure S1 Survival curves of patients carrying tumor protein p53 (TP53) mutations. (A) Overall survival (OS) of patients with different year of initial diagnosis according to tumor staging. (B) Disease free survival (DFS) in TP53 wild-type and mutated patients. (C) OS in stage I patients carrying wild-type or mutated TP53. (D) OS in stage II patients carrying wild-type or mutated TP53. (E) DFS in patients with wild-type and mutated TP53 subdivided according to mutation site. (F) DFS in patients with wild-type and mutated TP53 subdivided according to mutation type.

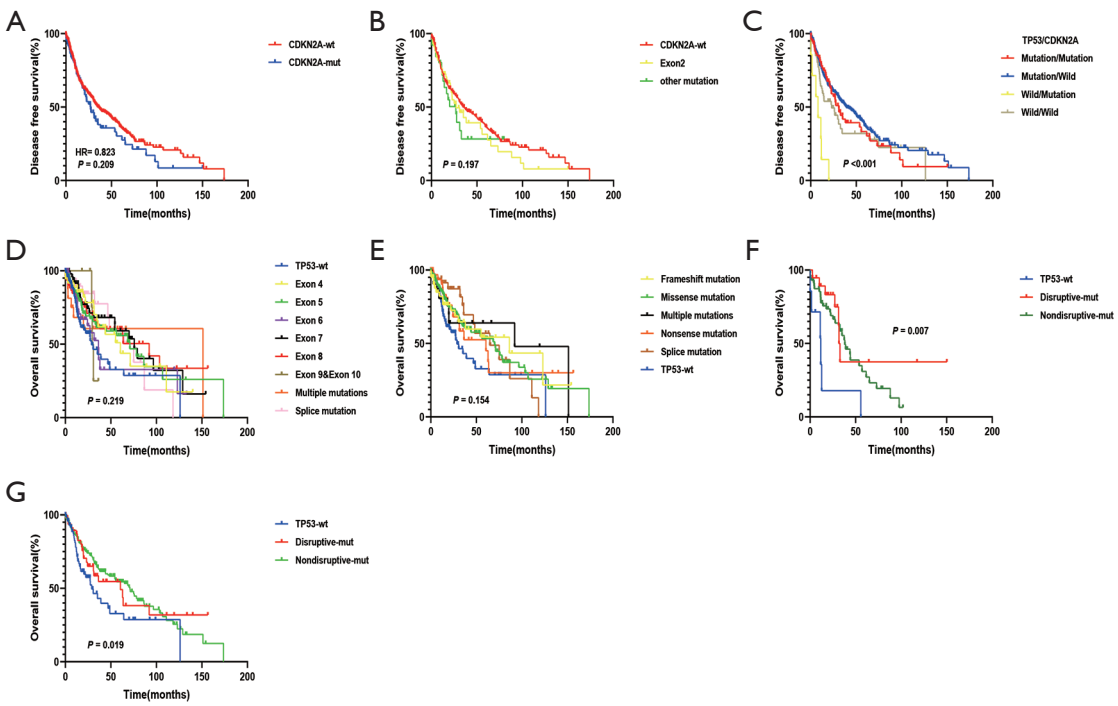

Figure S2 Survival curves of patients carrying cyclin dependent kinase inhibitor 2A (CDKN2A) and tumor protein p53 (TP53) mutations. (A) Disease free survival (DFS) in patients with wild-type and mutated CDKN2A. (B) DFS in patients with wild-type and mutated CDKN2A subdivided according to mutation site. (C) DFS of patients in different CDKN2A/TP53 mutation groups. (D) Overall survival (OS) of different TP53 mutation sites in CDKN2A wild-type patients. (E) OS of different CDKN2A mutation types in CDKN2A wild-type patients. (F) OS of patients with wild-type and mutated TP53 subdivided into disruptive or nondisruptive mutations in CDKN2A-mutated patients. (G) OS of CDKN2A wild-type patients with wild-type and mutated TP53 subdivided into disruptive or nondisruptive mutations.

https://dx.doi.org/10.21037/atm-21-3709

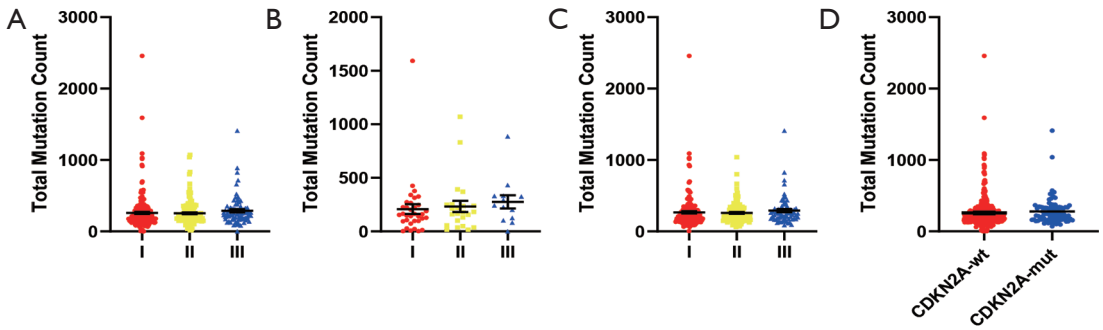

Figure S3 The mutation counts of LUSC patients. (A) Total mutation count of patients with lung squamous cell carcinoma (LUSC) at different tumor stages. (B) Total mutation count of TP53 wild-type patients with LUSC at different tumor stages. (C) Total mutation count of TP53-mutated patients with LUSC at different tumor stages. (D) Total mutation count of LUSC patients with wild-type and mutated CDKN2A. For (A-D), each dot represents a patient [mean ± standard deviation (SD)].

Table S1 1,021 gene panel

whole exons								
ABL1	ABL2	ACVR1B	AKT1	AKT2	AKT3	ALK	APC	AR
ARAF	ARID1A	ARID1B	ARID2	ASXL1	ATM	ATR	ATRX	AURKA
AURKB	AXIN1	AXIN2	AXL	B2M	BAP1	BARD1	BCL2	BCL2L1
BCOR	BLM	BMPR1A	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTK
C11orf30	CASP8	CBFB	CBL	CCND1	CCND2	CCND3	CCNE1	CD274
CDC73	CDH1	CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B	CDKN2A
CDKN2B	CDKN2C	CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL	CSF1R
CTCF	CTNNA1	CTNNB1	CUL3	CYLD	DAXX	DDR1	DDR2	DICER1
DNMT3A	EGFR	ELAC2	EME2	EP300	EPAS1	EPCAM	EPHA2	EPHA3
EPHA5	EPHB2	EPHB6	ERBB2	ERBB3	ERBB4	ERCC1	ERCC3	ERG
ERRFI1	ESR1	EXT1	EXT2	EZH2	FAM123B	FAM175A	FANCA	FANCC
FANCD2	FANCG	FANCM	FAS	FAT1	FAT2	FBXW7	FCGR2A	FCGR3A
FGFR1	FGFR2	FGFR3	FGFR4	FH	FLCN	FLT1	FLT3	FLT4
FOXA1	FOXL2	FOXP1	FUBP1	GAB2	GALNT12	GATA3	GNA11	GNAQ
GNAS	GRIN2A	HDAC1	HDAC4	HGF	HNF1A	HOXB13	HRAS	HSP90AA1
IDH1	IDH2	IFNG	IFNGR1	IGF1R	IL7R	INPP4B	IRF2	IRS2
JAK1	JAK2	JAK3	KDM5A	KDM5C	KDM6A	KDR	KEAP1	KIT
KRAS	LRP1B	MAP2K1	MAP2K2	MAP2K4	MAP3K1	MAPK1	MAX	MCL1
MDM2	MDM4	MED12	MEN1	MET	MITF	MLH1	MLH3	MLL
MLL2	MLL3	MPL	MRE11A	MS4A1	MSH2	MSH3	MSH6	MTOR
MUTYH	MYC	MYCL1	MYCN	MYD88	NBN	NCOR1	NDUFA13	NF1
NF2	NOTCH1	NOTCH2	NOTCH3	NOTCH4	NPM1	NRAS	NSD1	NTHL1

Table S1 (*continued*)

https://dx.doi.org/10.21037/atm-21-3709

Table S1 (*continued*)

whole exons								
NTRK1	NTRK3	PALB2	PAX5	PBRM1	PCK1	PDCD1LG2	PDGFRA	PDGFRB
PDK1	PHF6	PIK3CA	PIK3CB	PIK3CG	PIK3R1	PIK3R2	PMS1	PMS2
POLD1	POLE	POT1	PPM1D	PRKAR1A	PTCH1	PTCH2	PTEN	PTPN11
RAD50	RAD51	RAD51B	RAD51C	RAD51D	RAF1	RARA	RB1	RBM10
RET	RHEB	RHOA	RICTOR	RINT1	RNASEL	RNF43	ROS1	RPS6KB1
RUNX1	SDHA	SDHAF2	SDHB	SDHC	SDHD	SERPINB3	SERPINB4	SETD2
SLX4	SMAD2	SMAD4	SMARCA4	SMARCB1	SMARCE1	SMO	SOX2	SOX9
SRC	STAG2	STAT3	STK11	SUFU	SYK	TBX3	TCF7L2	TET2
TGFBR2	TMEM127	TMPRSS2	TNFAIP3	TOP1	TOP2A	TP53	TP73	TSC1
TSC2	VEGFA	VHL	WT1	XPO1	XRCC2	XRCC3	ZFHX3	ZMAT3
intron, promoter, fusion points/breakpoints								
ALK	BCL2L11	BRAF	BRCA1	BRD4	CD74	EGFR	EML4	ERG
ETV6	EZR	FGFR1	FGFR2	FGFR3	KIF5B	KIT	MAML2	MET
MSH2	MYC	MYCL1	NCOA4	NOTCH2	NTRK1	NTRK2	NTRK3	PDGFRA
PMS2	PPARG	RAF1	RET	ROS1	RSPO2	SLC34A2	TERT	TFE3
TMPRSS2	TPM3							
partial exons								
ABCA13	ABCB1	ABCC1	ABCC11	ABCC2	ABCG2	ACACA	ACIN1	ACTB
ACTG1	ACTG2	ACVR2A	ACVRL1	ADAM29	ADAMTS5	ADCY1	AFF1	AFF2
AFF3	AFF4	AHNAK	AKAP9	ALB	AMOT	ANGPT1	ANK3	ANKRD27
ANKRD30A	ANKRD30B	ANKRD36B	APEX1	APOBEC3B	ARAP3	ARFGEF1	ARFGEF2	ARHGAP26
ARHGAP29	ARHGAP35	ARID4B	ARNT	ASCL4	ASH1L	ASMTL	ASPM	ASTN1
ASXL2	ATIC	ATP12A	ATP11B	ATP1A1	ATP2B3	BAZ2B	BBS9	BCAS1
BCL11A	BCL11B	BCL2A1	BCL2L11	BCL3	BCL9	BCLAF1	BCORL1	BCR
BIRC2	BIRC3	BMPR2	BNC2	BPTF	BRD2	BRD3	BRSK1	BRWD1
BTLA	BUB1	C15orf23	C15orf55	C1QA	C1S	C3orf70	C7orf53	C8orf34
CACNA1D	CACNA1E	CADM2	CAMTA1	CAPN7	CARD11	CASP1	CASQ2	CBLB
CBR1	CBR3	CCDC168	CCNA1	CCNB3	CCT3	CCT5	CCT6B	CD22
CD33	CD5L	CDA	CDH11	CDH18	CDH23	CDK13	CHD1	CHD1L
CHD3	CHD4	CHD6	CHD8	CHD9	CHFR	CHI3L1	CHN1	CIITA
CKS1B	CLCC1	CLDN18	CLP1	CLSPN	CLTC	CNOT3	CNOT4	CNTN1
CNTN5	CNTNAP1	CNTNAP5	COL1A1	COL2A1	COL5A1	COL5A2	COL5A3	COPS2
CPS1	CREB3L1	CRIPAK	CRLF2	CRNKL1	CRTC1	CRYBG3	CSF1	CSF3R
CSMD1	CSMD3	CSNK1A1	CSNK1G3	CSNK2A1	CTLA4	CTNNA2	CTNND1	CUX1
CYBA	CYP19A1	CYP1B1	CYP1A1	CYP2A13	CYP2C19	CYP2C8	CYP2D6	CYP3A4

Table S1 (*continued*)

https://dx.doi.org/10.21037/atm-21-3709

Table S1 (*continued*)

whole exons								
CYP3A5	DCC	DDX3X	DDX5	DEK	DHX35	DHX9	DIAPH1	DIS3L2
DLC1	DMD	DNAH6	DNAJC11	DNM2	DNMT1	DOCK2	DOCK7	DOT1L
DPYD	DRGX	DTX1	DUSP22	DYSF	EBF1	ECT2L	EEF1A1	EGR3
EIF2AK3	EIF2C3	EIF3A	EIF4G3	ELF1	ELF3	ELF4	ELL	ELMO1
ELN	EMID2	EPC1	EPHA1	EPHA4	EPHA7	EPHB1	EPHB4	EPOR
EPPK1	EPS15	ERBB2IP	ERCC2	ESR2	ETS1	ETV1	ETV5	ETV6
EWSR1	EZR	F8	FAM131B	FAM135B	FAM157B	FAM22A	FAM46C	FAM5C
FAP	FASLG	FAT3	FAT4	FCGR1A	FCGR2B	FCRL4	FGF10	FGF14
FGF23	FGF3	FGF4	FGF6	FKBP5	FLG	FLI1	FLNC	FMN2
FMR1	FN1	FNDC4	FOXA2	FOXO3	FOXQ1	FRG1	FRMPD4	FUS
FXR1	FYN	FZD1	G3BP1	G3BP2	GABRA6	GATA2	GFRAL	GIGYF1
GKN2	GLB1L3	GLI1	GLI2	GLI3	GMPS	GNA12	GNA13	GNG2
GPC3	GPR124	GPX1	GRB7	GRM3	GSK3B	GSTM5	GSTP1	GUSB
H3F3A	H3F3C	HCLS1	HCN1	HDAC9	HECW1	HERC2	HEY1	HIP1
HIST1H1C	HIST1H1D	HIST1H1E	HIST1H2AC	HIST1H2AG	HIST1H2AL	HIST1H2AM	HIST1H2BC	HIST1H2BD
HIST1H2BJ	HIST1H2BK	HIST1H2BO	HIST1H3B	HIST1H4I	HLF	HMCN1	HNRPDL	HOXA11
HOXA13	HOXA3	HOXA9	HOXC13	HOXD11	HOXD13	HSD3B1	HSD3B2	HSP90AB1
HSPA8	HSPD1	HSPH1	ICK	IFITM1	IFITM3	IGF2	IGF2R	IGLL5
IGSF10	IKBKE	IKZF1	IKZF2	IKZF3	IL1RAPL1	IL21R	IL6	IL6ST
IMPG1	ING1	INHBA	INPP4A	INPP5D	INPPL1	IRF4	IRF6	ITGB3
ITK	ITSN1	JARID2	KALRN	KAT6A	KAT6B	KCNJ5	KCNQ2	KDM2B
KDM3B	KEL	KIF5B	KLB	KLF4	KLHL6	KLK1	KRTAP5-5	L3MBTL1
LAMA2	LCP1	LEF1	LGALS8	LIFR	LPHN2	LPP	LRP2	LRP4
LRP5	LRP6	LRRC7	LRRK2	LYN	LZTS1	MACF1	MAD1L1	MAGI2
MAGOH	MAML2	MAML3	MAP3K13	MAPK3	MCC	MCM3	MDH2	MECOM
MEF2C	MGA	MIB1	MIOS	MKI67	MKL1	MLL4	MLLT3	MLLT6
MMP2	MMP11	MN1	MNDA	MNX1	MPO	MSH4	MSN	MSR1
MTHFR	MTRR	MUC5B	MYB	MYBL2	MYH10	MYH11	MYH14	MYH9
MYO3A	NAP1L1	NAV3	NBPF1	NCAM2	NCF2	NCF4	NCK1	NCOA2
NCOR2	NCSTN	NDRG1	NEB	NFATC4	NFE2L2	NFE2L3	NIN	NKX3-1
NLRC3	NOD1	NOS3	NQO1	NR1I2	NR2F2	NR4A2	NRP2	NRXN1
NTM	NTRK2	NUMA1	NUP107	NUP210	NUP98	OBSCN	OGDH	OMD
OPCML	OR11G2	OR2T4	OR4A15	OR4C6	OR5L2	OR6F1	P2RY8	P4HB
PABPC1	PABPC3	PAG1	PAK1	PAK3	PARK2	PARP1	PASK	PAX3

Table S1 (*continued*)

https://dx.doi.org/10.21037/atm-21-3709

Table S1 (*continued*)

whole exons								
PAX7	PBX1	PC	PCDH18	PCLO	PCSK6	PCSK7	PDCD1	PDCD11
PDE4DIP	PDGFB	PDILT	PER1	PGR	PHF1	PIK3C2A	PIK3C2B	PIK3C2G
PIK3R3	PIP5K1A	PKD1L2	PKHD1	PLAC8	PLAG1	PLCB1	PLCG1	PLCG2
PLK1	PLXNA1	PLXNB2	POLQ	POLR2B	POM121	POM121L12	POTEG	POU2AF1
PPP1R17	PPP2R1A	PPP6C	PRAM1	PRDM1	PRDM16	PREX2	PRF1	PRKAA1
PRKCB	PRKCI	PRKDC	PRRX1	PRX	PSG2	PSIP1	PSMB1	PSMB5
PTGS1	PTGS2	PTK2	PTPN13	PTPN2	PTPRB	PTPRD	PTPRF	PTPRJ
PTPRK	PTPRO	PTPRT	PTPRU	RAB35	RAC1	RAC2	RAD21	RAD54B
RANBP2	RASA1	RASGRP1	RBL1	RECQL4	REL	RELN	RFC1	RGS3
RHOH	RHOT1	RIT1	RNF213	ROBO1	ROBO2	ROBO3	ROCK1	RPGR
RPL22	RPTOR	RSPO2	RSPO3	RUNX1T1	RUNX2	RXRA	RYR1	RYR2
SBDS	SCUBE2	SEC31A	SEMA3A	SEMA3E	SEMA6A	SERP2	SERPINA7	SETBP1
SETDB1	SF1	SF3A1	SF3A3	SF3B1	SFPQ	SGCZ	SH3PXD2A	SHH
SI	SIN3A	SLC16A1	SLC1A2	SLC22A16	SLC22A18	SLC22A2	SLC22A3	SLCO1B3
SLIT1	SLIT2	SMAD3	SMC1A	SMC1B	SMURF2	SNCAIP	SNTG1	SNX29
SOD2	SOS1	SOX10	SOX17	SPEN	SPOP	SPRR3	SPSB4	SPTA1
SRD5A2	SRGAP1	SRGAP3	SRSF2	SRSF7	SSX1	STAG1	STAT1	STAT5A
SUCLG1	SUCLG2	SULT1A1	SUZ12	SVEP1	SYNCRIP	SYNE1	TAF1	TAF15
TAF1L	TAL1	TBL1XR1	TBX15	TBX22	TCEB1	TCERG1	TCF12	TCF3
TCF4	TCL1A	TCP11	TEC	TENM3	TERT	TFDP1	TFDP2	TFE3
TGFBR1	TGFBR3	TGM2	THBS1	THBS2	THRAP3	TJP1	TLE1	TLL2
TLR4	TLX3	TMEM132D	TNN	TNPO1	TOP2B	TP53BP1	TP63	TPM3
TPR	TRAF5	TRERF1	TRIM24	TRIM58	TRIO	TRPC5	TRRAP	TSHR
TSHZ2	TSHZ3	TTF1	TTL	TUBA3C	TUBB3	TUSC3	TXNIP	TYMS
TYR	TYRP1	U2AF1	UBE2D2	UBR5	UGT1A1	UMPS	UPF3B	USH2A
USP6	USP8	VDAC2	VEZF1	VIM	WASF3	WDR90	WDTC1	WHSC1
WHSC1L1	WIPF1	WNK1	WNT5A	WSCD2	WWOX	WWP1	WWP2	XBP1
XPC	XRCC1	YBX1	YY1AP1	ZBTB16	ZC3H11A	ZFP36L1	ZFP36L2	ZFPM2
ZIC3	ZNF217	ZNF384	ZNF521	ZNF638	ZNF750	ZNF804B	ZNF814	
germline mutation								
ATM	BRCA1	BRCA2	MLH1	MLH3	MSH2			
MSH3	MSH6	PALB2	PMS1	PMS2				

https://dx.doi.org/10.21037/atm-21-3709

Table S2 Patient and tumor characteristics according to TP53 status

Variable	N	TP53 status		
		Mutation (n=409)	Wild (n=83)	P value
Age (years)				
<60	89	74	15	0.452
60-70	204	174	30	
>70	190	153	37	
Unknown	9	8	1	
Sex				
Male	363	307	56	0.152
Female	129	102	27	
Lymph node status				
pN0	316	265	51	0.695
pN1	130	105	25	
pN2/N3	46	39	7	
Tumor				
T1	110	87	23	0.355
T2	288	245	43	
T3	70	59	11	
T4	24	18	6	
Tumor stage				
I	239	198	41	0.682
II	160	132	28	
III	86	72	14	
IV	7	7	0	
Primary Tumor Site				
L-Upper	131	105	26	0.308
L-Lower	77	62	15	
R-Upper	128	107	21	
R-Middle	17	12	5	
R-Lower	108	96	12	
Bronchial	10	9	1	
Unknown	21	18	3	

Table S2 (*continued*)

https://dx.doi.org/10.21037/atm-21-3709

Table S2 (*continued*)

Variable	N	TP53 status		
		Mutation (n=409)	Wild (n=83)	P value
Year Initial Diagnosis				
–2000	30	24	6	0.583
2001–2005	96	85	11	
2006–2010	182	151	31	
2011–	167	135	32	
Unknown	17	14	3	
Surgical Margin Resection Status				
R0	390	326	64	0.862
R1+R2	17	14	3	
Unknown	85	69	16	
CDKN2A Mutation status				
Wild type	406	331	75	0.040
Mutated type	86	78	8	

https://dx.doi.org/10.21037/atm-21-3709

Table S3 Patient and tumor characteristics according to CDKN2A status

Variable	N	CDKN2A status		
		Mutation (n=86)	Wild (n=406)	P value
Age (years)				
<60	89	20	69	0.553
60-70	210	34	176	
>70	184	30	154	
Unknown	9	2	7	
Sex				
Male	363	65	298	0.418
Female	129	21	108	
Lymph node status				
pN0	316	53	263	0.225
pN1	130	28	102	
pN2/N3	46	5	41	
Tumor				
T1	110	17	93	0.844
T2	288	53	235	
T3	70	11	59	
T4	24	5	19	
Tumor stage				
I	239	38	201	0.344
II	160	34	126	
III	86	12	74	
IV	7	2	5	
Primary Tumor Site				
L-Upper	131	20	111	0.332
L-Lower	77	13	64	
R-Upper	128	22	106	
R-Middle	17	1	16	
R-Lower	108	20	88	
Bronchial	10	3	7	
Unknown	21	7	14	

https://dx.doi.org/10.21037/atm-21-3709