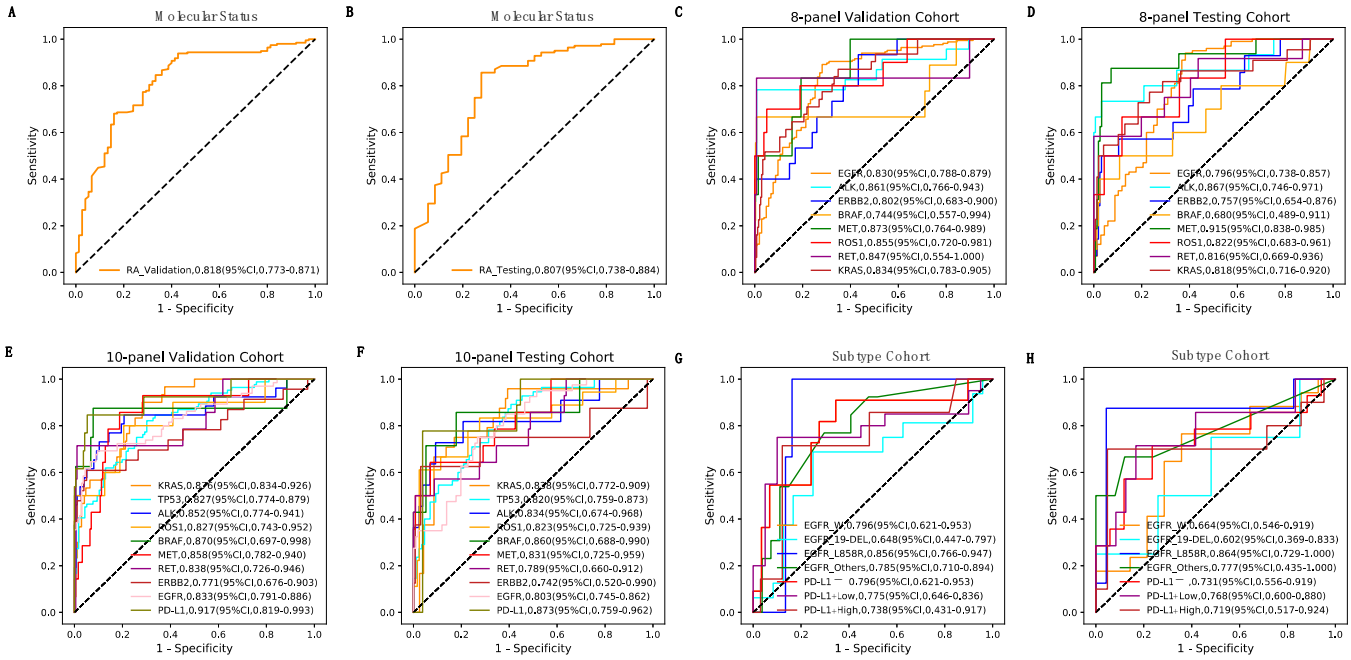

Figure S1. The radiomics model performances in the prediction of multiple molecular alterations. (**A**,**B**) The ROC curves for predicting target molecular status (positive-type and negative-type) in the validation set and testing set, respectively. (**C**,**D**) The ROC curves for predicting multiple mutations in the 8-panel cohort in the validation set and testing set, respectively. (**E**,**F**) The ROC curves for predicting multiple alterations in the 10-panel cohort in the validation set and testing set, respectively. (**G**,**H**) The ROC curves for predicting molecular ex-pression in the subtype cohort in the validation set and testing set, respectively, EGFR_W and PD-L1- represent wild-type of EGFR and negative expression of PD-L1. PD-L1+ was separated into PD-L1+ Low and PD-L1+ High according to the TPS cutoff of 50%.

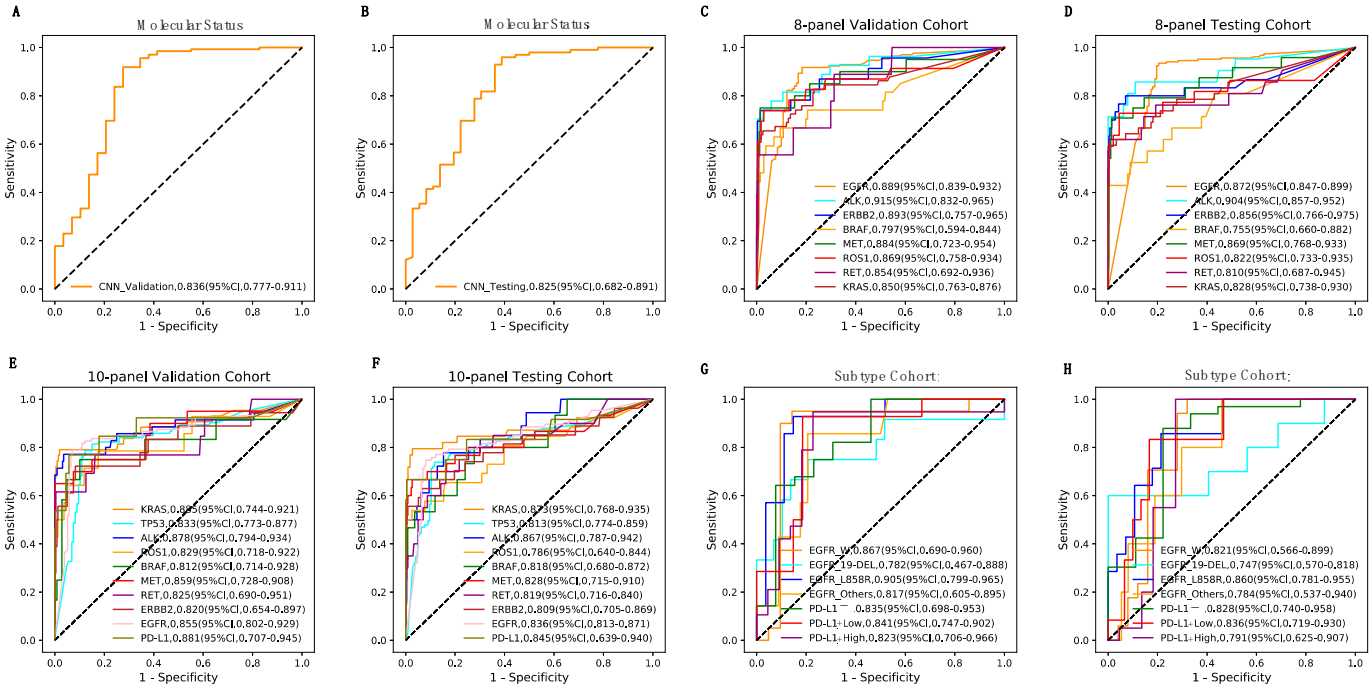

Figure S2. The CNN-based deep learning model performances in the prediction of multiple molecular alterations. (**A**,**B**) The ROC curves for predicting target molecular status (positive-type and negative-type) in the validation set and testing set, respectively. (**C**,**D**) The ROC curves for predicting multiple mutations in the 8-panel cohort in the validation set and testing set, respectively. (**E**,**F**) The ROC curves for predicting multiple alterations in the 10-panel cohort in the validation set and testing set, respectively. (**G**,**H**) The ROC curves for predicting molecular ex-pression in the subtype cohort in the validation set and testing set, respectively, EGFR_W and PD-L1- represent wild-type of EGFR and negative expression of PD-L1. PD-L1+ was separated into PD-L1+ Low and PD-L1+ High according to the TPS cutoff of 50%.

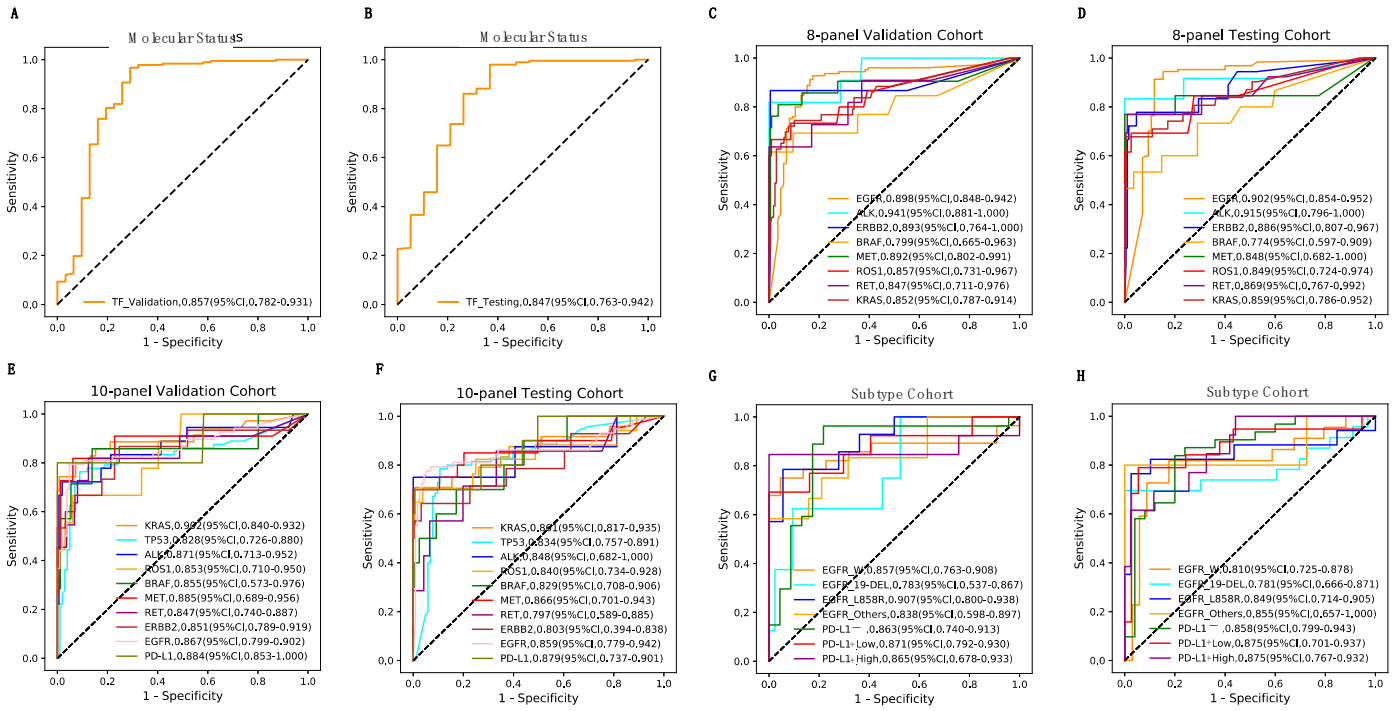

Figure S3. The transformer-based deep learning model performances in the prediction of multiple molecular alterations. (**A**,**B**) The ROC curves for predicting target molecular status (positive-type and negative-type) in the validation set and testing set, respectively. (**C**,**D**) The ROC curves for predicting multiple mutations in the 8-panel cohort in the validation set and testing set, respectively. (**E**,**F**) The ROC curves for predicting multiple alterations in the 10-panel cohort in the validation set and testing set, respectively. (**G**,**H**) The ROC curves for predicting molecular ex-pression in the subtype cohort in the validation set and testing set, respectively, EGFR_W and PD-L1- represent wild-type of EGFR and negative expression of PD-L1. PD-L1+ was separated into PD-L1+ Low and PD-L1+ High according to the TPS cutoff of 50%.

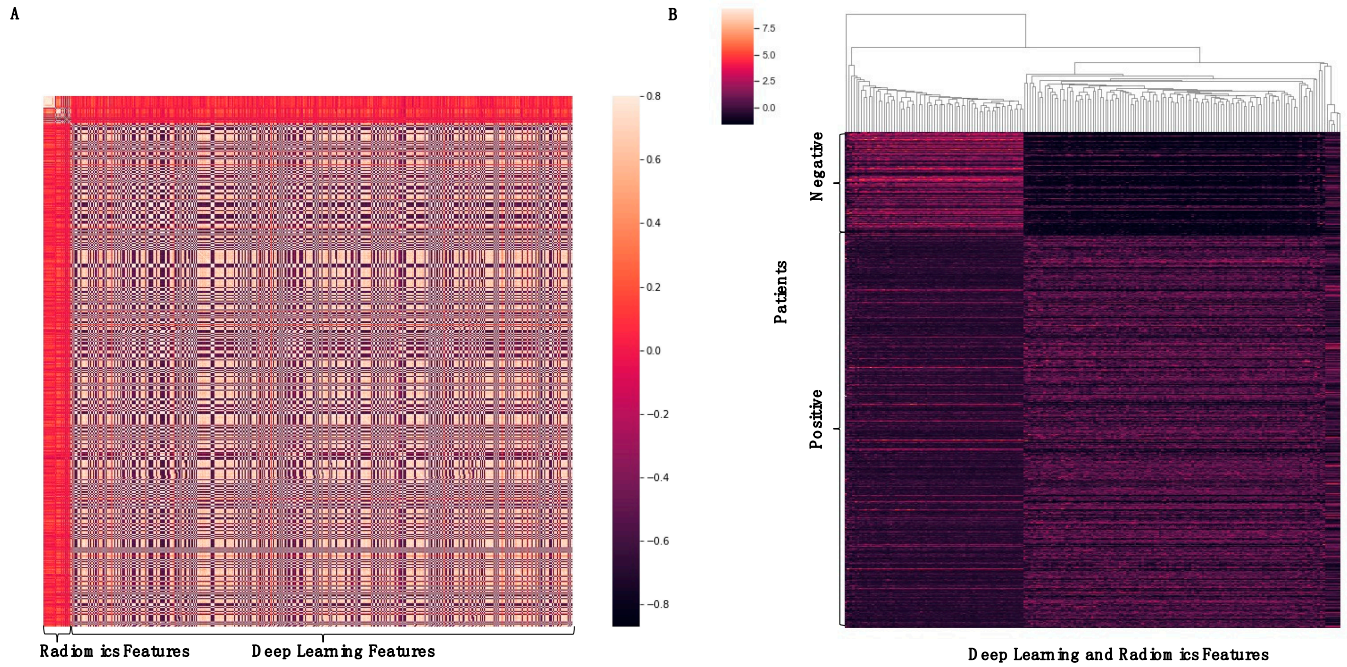

Figure S4. Association between radiomics and deep learning features. (**A**) Correlation heatmap of radiomics and deep learning features. (**B**) The correlation between selected features and the mutant genotypes patients in the development cohorts.

Table S1. The clinical characteristic of cancer shared dataset.

	All Patients N = 1096	**8-Panel Cohort N = 932**	**10-Panel Cohort N = 637**
Age (SD)	58.26 (10.69)	58.11 (10.64)	58.26 (11.03)
Sex			
Male	598(54.6%)	481(51.6%)	393(61.7%)
Female	498(45.4%)	451(48.4%)	244(38.3%)
Smoking history			
Current or former	441(40.2%)	346(37.1%)	315(49.5%)
Never	581(53.0%)	525(56.3%)	317(49.8%)
Unknow	74(6.8%)	61(6.5%)	5(0.8%)
Histology type			
LUAD	875(79.8%)	786(84.3%)	517(81.2%)
LUSC	96(8.8%)	48(5.2%)	73(11.5%)
Others	125(11.4%)	98(10.5%)	47(7.4%)
Actional mutation			
EGFR			
Mutant	585(53.4%)	585(62.8%)	260(40.8%)
Wild	511(46.6%)	347(37.2%)	377(59.2%)
ALK			
Mutant	99(9.0%)	99(10.6%)	82(12.9%)
Wild	997(91.0%)	833(89.4%)	555(87.1%)
ERBB2			
Mutant	82(7.5%)	82(8.8%)	63(9.9%)
Wild	1014(92.5%)	850(91.2%)	574(90.1%)
BRAF			
Mutant	43(3.9%)	43(4.6%)	34(5.3%)
Wild	1053(96.1%)	889(95.4%)	603(94.7%)

MET			
Mutant	74(6.8%)	74(7.9%)	61(9.6%)
Wild	1022(93.2%)	858(92.1%)	576(90.4%)
ROS1			
Mutant	43(3.9%)	43(4.6%)	37(5.8%)
Wild	1053(96.1%)	889(95.4%)	600(94.2%)
RET			
Mutant	46(4.2%)	46(4.9%)	38(6.0%)
Wild	1050(95.8%)	886(95.1%)	599(94.0%)
KRAS			
Mutant	140(12.8%)	140(15.0%)	116(18.2%)
Wild	956(87.2%)	792(85.0%)	521(81.8%)
TP53			
Mutant	315(28.7%)	-	315(49.5%)
Wild	322(29.4%)	-	322(50.5%)
Unknown	459(41.9%)	-	-
PD-L1 Expression			
Positive	335 (30.6%)	-	212(33.3%)
Negative	432(39.4%)	-	425(66.7%)
Unknown	329(30.0%)	-	-

Abbreviations: LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma.