

Appendix 1: ^{18}F -FDG PET/CT imaging protocol

Three different PET/CT scanners were used in Cohort A: Scanner A (n=83), Discovery 710 PET/CT scanner (General Electric Medical Systems); Scanner B (n=31), Biograph LSO Sensation 16 PET/CT scanner (Siemens Medical Solutions); Scanner C (n=25), PoleStar m660 PET/CT scanner (SinoUnion). The PET scan was obtained from the skull base to the proximal thighs after an initial low-dose CT. PET images were reconstructed using four iterative algorithms respectively [Scanner A: 3D-ordered subset expectation maximization (OSEM) algorithm with time-of-flight (TOF) and PSF correction, 128×128 matrix, voxel size 3.91×3.91×3.27 mm³; Scanner B: OSEM algorithm with TOF, 4 iterations, 8 subsets, 128×128 matrix, voxel size 5×5×5.3 mm³; Scanner C: OSEM

algorithm with TOF, 2 iterations, 10 subsets, 192×192 matrix, 3.15×3.15×1.87 mm³]. On PET images, all the ROIs were resampled into 3×3×3 mm³. Voxel intensities were resampled with 64 discrete values between 0 and 30 SUV units. On the CT images, all the ROIs were resampled into 1×1×1 mm³. Hounsfield units were resampled with 400 discrete values between -1,000 and 3,000 Hounsfield units.

Appendix 2: laboratory inflammatory parameters calculation method

The calculation method was as followed:

- (I) dNLR = neutrophil/(leukocyte-neutrophil);
- (II) PLR = platelet/lymphocyte;
- (III) SII = platelet × neutrophil/lymphocyte.

Table S1 Radiomics features extracted from the PET and CT images according to the formulas described in the manual of LIFEx 7.4.0 software (<https://www.lifexsoft.org/>)

Radiomics features

PET-MORPHOLOGICAL features

MORPHOLOGICAL Volume

MORPHOLOGICAL Approximate Volume

MORPHOLOGICAL Surface Area

MORPHOLOGICAL Surface to Volume Ratio

MORPHOLOGICAL Compactness1

MORPHOLOGICAL Compactness2

MORPHOLOGICAL Spherical Disproportion

MORPHOLOGICAL Sphericity

MORPHOLOGICAL Asphericity

MORPHOLOGICAL Centre of Mass Shift

MORPHOLOGICAL Maximum 3D Diameter

MORPHOLOGICAL Integrated Intensity

PET-first order features

INTENSITY BASED Mean SUVbw

INTENSITY BASED Variance SUVbw

INTENSITY BASED Skewness SUVbw

INTENSITY BASED Kurtosis SUVbw

INTENSITY BASED Median SUVbw

INTENSITY BASED Minimum Grey Level SUVbw

INTENSITY BASED 10thPercentile SUVbw

INTENSITY BASED 50thPercentile SUVbw

INTENSITY BASED 90thPercentile SUVbw

INTENSITY BASED Maximum Grey Level SUVbw

INTENSITY BASED Interquartile Range SUVbw

INTENSITY BASED Range SUVbw

INTENSITY BASED Mean Absolute Deviation SUVbw

INTENSITY BASED Robust Mean Absolute Deviation SUVbw

INTENSITY BASED Median Absolute Deviation SUVbw

INTENSITY BASED Coefficient of Variation SUVbw

INTENSITY BASED Quartile Coefficient of Dispersion SUVbw

INTENSITY BASED Energy SUVbw

INTENSITY BASED Root Mean Square SUVbw

Table S1 (continued)

Table S1 (continued)

Intensity Histogram Intensity Histogram Mean SUVbw

Intensity Histogram Variance SUVbw

Intensity Histogram Skewness SUVbw

Intensity Histogram Kurtosis SUVbw

Intensity Histogram Median SUVbw

Intensity Histogram Minimum Grey Level SUVbw

Intensity Histogram 10th Percentile SUVbw

Intensity Histogram 90th Percentile SUVbw

Intensity Histogram Maximum Grey Level SUVbw

Intensity Histogram Mode SUVbw

Intensity Histogram Interquartile Range SUVbw

Intensity Histogram Range SUVbw

Intensity Histogram Mean Absolute Deviation SUVbw

Intensity Histogram Robust Mean Absolute Deviation SUVbw

Intensity Histogram Median Absolute Deviation SUVbw

Intensity Histogram Coefficient of Variation SUVbw

Intensity Histogram Quartile Coefficient of Dispersion SUVbw

Intensity Histogram EntropyLog2 SUVbw

Intensity Histogram Uniformity SUVbw

Intensity Histogram Maximum Histogram Gradient SUVbw

Intensity Histogram Maximum Histogram Gradient Grey Level SUVbw

Intensity Histogram Minimum Histogram Gradient SUVbw

Intensity Histogram Minimum Histogram Gradient Grey Level SUVbw

PET-texture features

GLCM

GLCM Joint Maximum

GLCM Joint Average

GLCM Joint Variance

GLCM Joint EntropyLog2

GLCM Difference Average

GLCM Difference Variance

GLCM Difference Entropy

GLCM Sum Average

GLCM Sum Variance

Table S1 (continued)

Table S1 (continued)

GLCM Sum Entropy
GLCM Angular Second Moment
GLCM Contrast
GLCM Dissimilarity
GLCM Inverse Difference
GLCM Normalised Inverse Difference
GLCM Inverse Difference Moment
GLCM Normalised Inverse Difference Moment
GLCM Inverse Variance
GLCM Correlation
GLCM Autocorrelation
GLCM Cluster Tendency
GLCM Cluster Shade
GLCM Cluster Prominence
GLRLM
GLRLM SRE
GLRLM LRE
GLRLM LGRE
GLRLM HGRE
GLRLM SRLGE
GLRLM SRHGE
GLRLM LRLGE
GLRLM LRHGE
GLRLM GLNUr
GLRLM RLNU
GLRLM RP
NGLDM
NGTDM Coarseness
NGTDM Contrast
NGTDM Busyness
NGTDM Complexity
NGTDM Strength
GLZLM
GLZLM SZE
GLZLM LZE

Table S1 (continued)

Table S1 (continued)

GLZLM LGZE
GLZLM HGZE
GLZLM SZLGE
GLZLM SZHGE
GLZLM LZLGE
GLZLM LZHGE
GLZLM GLNUz
GLZLM ZLNU
GLZLM ZP
GLSZM NZLNU
GLSZM GLV
GLSZM ZSV
GLSZM ZSE
CT-MORPHOLOGICAL features
MORPHOLOGICAL_Volume.IBSI.RNU0..1
MORPHOLOGICAL_ApproximateVolume.IBSI.YEKZ..1
MORPHOLOGICAL_voxelsCounting.IBSI.No..1
MORPHOLOGICAL_SurfaceArea.IBSI.C0JK..1
MORPHOLOGICAL_SurfaceToVolumeRatio.IBSI.2PR5..1
MORPHOLOGICAL_Compacity.IBSI.No..1
MORPHOLOGICAL_Compactness1.IBSI.SKGS..1
MORPHOLOGICAL_Compactness2.IBSI.BQWJ..1
MORPHOLOGICAL_SphericalDisproportion.IBSI.KRCK..1
MORPHOLOGICAL_Sphericity.IBSI.QCFX..1
MORPHOLOGICAL_Asphericity.IBSI.25C7..1
MORPHOLOGICAL_CentreOfMassShift.IBSI.KLMA..1
MORPHOLOGICAL_Maximum3DDiameter.IBSI.L0JK..1
MORPHOLOGICAL_IntegratedIntensity.IBSI.99N0..1
CT-first order features
INTENSITY.BASED_Mean.HU.IBSI.Q4LE
INTENSITY.BASED_Variance.HU.IBSI.ECT3
INTENSITY.BASED_Skewness.HU.IBSI.KE2A
INTENSITY.BASED_Kurtosis.HU.IBSI.IPH6
INTENSITY.BASED_Median.HU.IBSI.Y12H
INTENSITY.BASED_MinimumGreyLevel.HU.IBSI.1GSF

Table S1 (continued)

Table S1 (continued)

INTENSITY.BASED_10thPercentile.HU.IBSI.QG58
INTENSITY.BASED_25thPercentile.HU.IBSI.No
INTENSITY.BASED_50thPercentile.HU.IBSI.Y12H
INTENSITY.BASED_75thPercentile.HU.IBSI.No
INTENSITY.BASED_90thPercentile.HU.IBSI.8DWT
INTENSITY.BASED_StandardDeviation.HU.IBSI.No
INTENSITY.BASED_MaximumGreyLevel.HU.IBSI.84IY
INTENSITY.BASED_InterquartileRange.HU.IBSI.SALO
INTENSITY.BASED_Range.HU.IBSI.2OJQ
INTENSITY.BASED_MeanAbsoluteDeviation.HU.IBSI.4FUA
INTENSITY.BASED_RobustMeanAbsoluteDeviation. HU.IBSI.1128
INTENSITY.BASED_MedianAbsoluteDeviation.HU.IBSI.N72L
INTENSITY.BASED_CoefficientOfVariation.HU.IBSI.7TET
INTENSITY.BASED_QuartileCoefficientOfDispersion. HU.IBSI.9S40
INTENSITY.BASED_Energy.HU.IBSI.N8CA
INTENSITY.BASED_RootMeanSquare.HU.IBSI.5ZWQ
INTENSITY.BASED_TotalLesionGlycolysis.HU.IBSI.No
INTENSITY.HISTOGRAM_IntensityHistogramMean.HU.IBSI. X6K6
INTENSITY.HISTOGRAM_IntensityHistogramVariance. HU.IBSI.CH89
INTENSITY.HISTOGRAM_IntensityHistogramSkewness. HU.IBSI.88K1
INTENSITY.HISTOGRAM_IntensityHistogramKurtosis. HU.IBSI.C3I7
INTENSITY.HISTOGRAM_IntensityHistogramMedian. HU.IBSI.WIFQ
INTENSITY.HISTOGRAM_ IntensityHistogramMinimumGreyLevel.HU.IBSI.1PR8
INTENSITY.HISTOGRAM_IntensityHistogram10thPercentile. HU.IBSI.GPMT
INTENSITY.HISTOGRAM_IntensityHistogram25thPercentile. HU.IBSI.No
INTENSITY.HISTOGRAM_IntensityHistogram50thPercentile. HU.IBSI.No
INTENSITY.HISTOGRAM_IntensityHistogram75thPercentile. HU.IBSI.No

Table S1 (continued)**Table S1** (continued)

INTENSITY.HISTOGRAM_IntensityHistogram90thPercentile. HU.IBSI.OZ0C
INTENSITY.HISTOGRAM_ IntensityHistogramStandardDeviation.HU.IBSI.No
INTENSITY.HISTOGRAM_ IntensityHistogramMaximumGreyLevel.HU.IBSI.3NCY
INTENSITY.HISTOGRAM_IntensityHistogramMode.HU.IBSI. AMMC
INTENSITY.HISTOGRAM_ IntensityHistogramInterquartileRange.HU.IBSI.WR00
INTENSITY.HISTOGRAM_IntensityHistogramRange. HU.IBSI.5Z3W
INTENSITY.HISTOGRAM_ IntensityHistogramMeanAbsoluteDeviation.HU.IBSI.D2ZX
INTENSITY.HISTOGRAM_ IntensityHistogramRobustMeanAbsoluteDeviation.HU.IBSI. WRZB
INTENSITY.HISTOGRAM_ IntensityHistogramMedianAbsoluteDeviation.HU.IBSI.4RNL
INTENSITY.HISTOGRAM_ IntensityHistogramCoefficientOfVariation.HU.IBSI.CWYJ
INTENSITY.HISTOGRAM_ IntensityHistogramQuartileCoefficientOfDispersion.HU.IBSI. SLWD
INTENSITY.HISTOGRAM_IntensityHistogramEntropyLog10. HU.IBSI.No
INTENSITY.HISTOGRAM_IntensityHistogramEntropyLog2. HU.IBSI.TLU2
INTENSITY.HISTOGRAM_AreaUnderCurveCsh.HU.IBSI.No
INTENSITY.HISTOGRAM_Uniformity.HU.IBSI.BJ5W
INTENSITY.HISTOGRAM_RootMeanSquare.HU.IBSI.No
INTENSITY.HISTOGRAM_MaximumHistogramGradient. HU.IBSI.12CE
INTENSITY.HISTOGRAM_ MaximumHistogramGradientGreyLevel.HU.IBSI.8E60
INTENSITY.HISTOGRAM_MinimumHistogramGradient. HU.IBSI.VQB3
INTENSITY.HISTOGRAM_ MinimumHistogramGradientGreyLevel.HU.IBSI.RHQZ
CT-texture features
GLCM
GLCM_JointMaximum.IBSI.GYBY.

Table S1 (continued)

Table S1 (continued)

GLCM_JointAverage.IBSI.60VM.
GLCM_JointVariance.IBSI.UR99.
GLCM_JointEntropyLog2.IBSI.TU9B.
GLCM_JointEntropyLog10.IBSI.No.
GLCM_DifferenceAverage.IBSI.TF7R.
GLCM_DifferenceVariance.IBSI.D3YU.
GLCM_DifferenceEntropy.IBSI.NTRS.
GLCM_SumAverage.IBSI.ZGXS.
GLCM_SumVariance.IBSI.OEEB.
GLCM_SumEntropy.IBSI.P6QZ.
GLCM_AngularSecondMoment.IBSI.8ZQL.
GLCM_Contrast.IBSI.ACUI.
GLCM_Dissimilarity.IBSI.8S9J.
GLCM_InverseDifference.IBSI.IB1Z.
GLCM_NormalisedInverseDifference.IBSI.NDRX.
GLCM_InverseDifferenceMoment.IBSI.WF0Z.
GLCM_NormalisedInverseDifferenceMoment.IBSI.1QCO.
GLCM_InverseVariance.IBSI.E8JP.
GLCM_Correlation.IBSI.NI2N.
GLCM_Autocorrelation.IBSI.QWB0.
GLCM_ClusterTendency.IBSI.DG8W.
GLCM_ClusterShade.IBSI.7NFM.
GLCM_ClusterProminence.IBSI.AE86.
GLRLM
GLRLM_ShortRunsEmphasis.IBSI.22OV.
GLRLM_LongRunsEmphasis.IBSI.W4KF.
GLRLM_LowGreyLevelRunEmphasis.IBSI.V3SW.
GLRLM_HighGreyLevelRunEmphasis.IBSI.G3QZ.
GLRLM_ShortRunLowGreyLevelEmphasis.IBSI.HTZT.
GLRLM_ShortRunHighGreyLevelEmphasis.IBSI.GD3A.
GLRLM_LongRunLowGreyLevelEmphasis.IBSI.IVPO.
GLRLM_LongRunHighGreyLevelEmphasis.IBSI.3KUM.
GLRLM_GreyLevelNonUniformity.IBSI.R5YN.
GLRLM_RunLengthNonUniformity.IBSI.W92Y.
GLRLM_RunPercentage.IBSI.9ZK5.

Table S1 (continued)

Table S1 (continued)

NGLDM
NGTDM_Coarseness.IBSI.QCDE.
NGTDM_Contrast.IBSI.65HE.
NGTDM_Busyness.IBSI.NQ30.
NGTDM_Complexity.IBSI.HDEZ.
NGTDM_Strength.IBSI.1X9X.
GLZLM
GLSZM_SmallZoneEmphasis.IBSI.5QRC.
GLSZM_LargeZoneEmphasis.IBSI.48P8.
GLSZM_LowGrayLevelZoneEmphasis.IBSI.XMSY.
GLSZM_HighGrayLevelZoneEmphasis.IBSI.5GN9.
GLSZM_SmallZoneLowGreyLevelEmphasis.IBSI.5RAI.
GLSZM_SmallZoneHighGreyLevelEmphasis.IBSI.HW1V.
GLSZM_LargeZoneLowGreyLevelEmphasis.IBSI.YH51.
GLSZM_LargeZoneHighGreyLevelEmphasis.IBSI.J17V.
GLSZM_GreyLevelNonUniformity.IBSI.JNSA.
GLSZM_NormalisedGreyLevelNonUniformity.IBSI.Y1RO.
GLSZM_ZoneSizeNonUniformity.IBSI.4JP3.
GLSZM_NormalisedZoneSizeNonUniformity.IBSI.VB3A.
GLSZM_ZonePercentage.IBSI.P30P.
GLSZM_GreyLevelVariance.IBSI.BYLV.
GLSZM_ZoneSizeVariance.IBSI.3NSA.
GLSZM_ZoneSizeEntropy.IBSI.GU8N.

PET, positron emission tomography; CT, computed tomography; GLCM, grey level co-occurrence matrix; GLRLM, grey-level run length matrix; SRE, short-run emphasis; LRE, long-run emphasis; LGRE, low gray-level run emphasis; HGRE, high gray-level run emphasis; SRLGE, short-run low gray-level emphasis; SRHGE, short-run high gray-level emphasis; LRLGE, long-run low gray-level emphasis; LRHGE, long-run high gray-level emphasis; GLNUr, gray-level non-uniformity for run; RLNU, run length non-uniformity; RP, run percentage; NGLDM, neighborhood grey-level different matrix; GLZLM, grey-level zone length matrix; SZE, short-zone emphasis; LZE, large-zone emphasis; LGZE, low gray-level zone emphasis; HGZE, high gray-level zone emphasis; SZLGE, small-zone low gray-level emphasis; SZHGE, small-zone high gray-level emphasis; LZLGE, large-zone low gray-level emphasis; LZHGE, large-zone high gray-level emphasis; GLNUz, gray-level non-uniformity for zone; ZLNU, zone size non-uniformity; ZP, zone percentage; NZLNU, normalized zone size non-uniformity; GLV, grey level variance; ZSV, zone size variance; ZSE, zone size entropy.

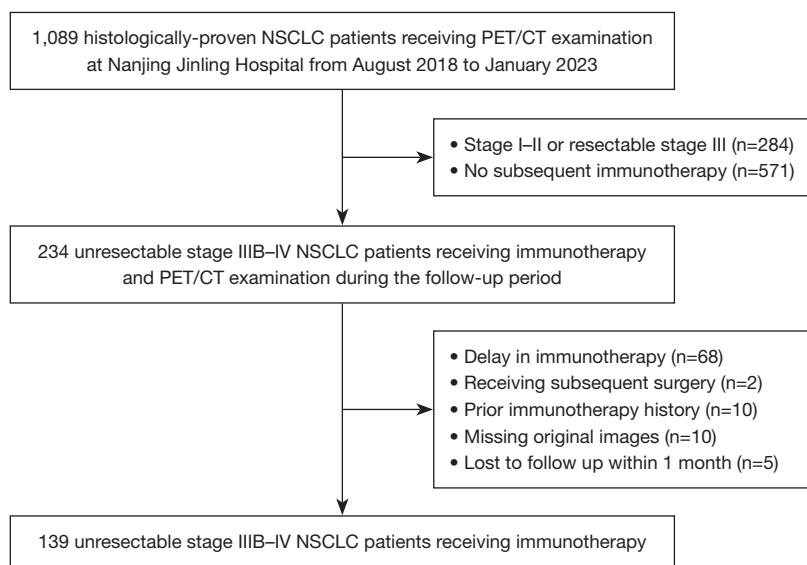


Figure S1 Flowchart of patient selection in Cohort A. NSCLC, non-small cell lung cancer; PET, positron emission tomography; CT, computed tomography.

Table S2 List of variables entering clustering analysis with P<0.1 by Cox regression analysis for PFS

Variables	HR (95% CI)	P value
MORPHOLOGICAL_Volume.IBSI.RNU0.	1.18 (0.98–1.43)	0.08
MORPHOLOGICAL_ApproximateVolume.IBSI.YEKZ.	1.18 (0.98–1.43)	0.08
MORPHOLOGICAL_SurfaceArea.IBSI.C0JK.	1.22 (1.02–1.47)	0.03
MORPHOLOGICAL_Compacity.IBSI.No.	1.25 (1.02–1.52)	0.03
MORPHOLOGICAL_Compactness1.IBSI.SKGS.	0.78 (0.64–0.96)	0.02
MORPHOLOGICAL_Compactness2.IBSI.BQWJ.	0.77 (0.63–0.95)	0.02
MORPHOLOGICAL_SphericalDisproportion.IBSI.KRCK.	1.25 (1.03–1.52)	0.03
MORPHOLOGICAL_Sphericity.IBSI.QCFX.	0.79 (0.64–0.96)	0.02
MORPHOLOGICAL_Asphericity.IBSI.25C7.	1.25 (1.03–1.52)	0.03
MORPHOLOGICAL_CentreOfMassShift.IBSI.KLMA.	1.26 (1.02–1.57)	0.04
MORPHOLOGICAL_Maximum3DDiameter.IBSI.L0JK.	1.31 (1.07–1.61)	0.01
MORPHOLOGICAL_IntegratedIntensity.IBSI.99N0.	1.24 (1.00–1.52)	0.045
INTENSITY.BASED_Skewness.SUVbw.IBSI.KE2A	1.35 (1.07–1.69)	0.01
INTENSITY.BASED_Kurtosis.SUVbw.IBSI.IPH6	1.37 (1.10–1.70)	0.005
INTENSITY.BASED_QuartileCoefficientOfDispersion.SUVbw.IBSI.9S40	0.78 (0.63–0.98)	0.03
INTENSITY.BASED_TotalLesionGlycolysis.SUVbw.IBSI.No	1.24 (1.01–1.52)	0.04
INTENSITY.HISTOGRAM_IntensityHistogramSkewness.SUVbw.IBSI.88K1	1.27 (0.98–1.64)	0.08
INTENSITY.HISTOGRAM_IntensityHistogramKurtosis.SUVbw.IBSI.C3I7	1.30 (1.07–1.57)	0.008
INTENSITY.HISTOGRAM_IntensityHistogramQuartileCoefficientOfDispersion.SUVbw.IBSI.SLWD	0.83 (0.68–1.02)	0.08
INTENSITY.BASED_90thPercentile.HU.IBSI.8DWT	1.30 (1.00–1.69)	0.053
INTENSITY.HISTOGRAM_IntensityHistogram90thPercentile.HU.IBSI.OZ0C	1.34 (1.03–1.75)	0.03
GLCM_InverseVariance.IBSI.E8JP.	1.42 (1.17–1.71)	<0.001
GLCM_ClusterShade.IBSI.7NFM.	0.80 (0.63–1.01)	0.06
GLRLM_LowGreyLevelRunEmphasis.IBSI.V3SW.	1.27 (1.00–1.62)	0.049
GLRLM_ShortRunLowGreyLevelEmphasis.IBSI.HTZT.	1.26 (0.99–1.60)	0.07
GLRLM_LongRunLowGreyLevelEmphasis.IBSI.IVPO.	1.28 (1.01–1.60)	0.047

PFS, progression-free survival; HR, hazard ratio; CI, confidence interval.

Table S3 Univariate analysis and multivariate stepwise Cox regression analysis for PFS and OS

Parameters	PFS				OS			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age >65 years	0.85 (0.56–1.28)	0.43	–	–	0.99 (0.57–1.70)	0.965	–	–
Smoking (yes)	0.80 (0.51–1.25)	0.33	–	–	0.72 (0.41–1.25)	0.239	–	–
Histology (squamous)	1.66 (1.08–2.55)	0.02*	1.63 (1.06–2.52)	0.03*	1.70 (0.98–2.93)	0.057	1.75 (1.01–3.02)	0.046*
Gender (male)	0.95 (0.55–1.67)	0.87	–	–	1.00 (0.51–1.96)	0.989	–	–
Brain metastases	1.04 (0.52–2.07)	0.91	–	–	0.70 (0.25–1.94)	0.490	–	–
Bone metastases	1.32 (0.85–2.05)	0.21	–	–	1.50 (0.86–2.60)	0.151	–	–
Liver metastases	1.89 (1.03–3.48)	0.04*	2.18 (1.18–4.05)	0.01*	2.74 (1.33–5.64)	0.006*	2.81 (1.32–5.98)	0.007*
Number of FDG-avid lesions >10	1.72 (1.10–2.70)	0.02*	–	–	1.78 (1.01–3.12)	0.046*	–	–
Immunotherapy line >1	1.16 (0.56–2.40)	0.70	–	–	1.10 (0.44–2.77)	0.083	–	–
Combination regimen			–	–			–	–
Chemotherapy	Reference		–	–	Reference		–	–
Anti-angiogenesis	1.85 (0.80–4.31)	0.15	–	–	1.01 (0.31–3.27)	0.993	–	–
None	1.06 (0.52–2.14)	0.87	–	–	1.67 (0.81–3.45)	0.162	–	–
dNLR >3	1.47 (0.88–2.44)	0.14	–	–	1.89 (1.02–3.48)	0.042*	–	–
SII >1,270	1.07 (0.66–1.74)	0.77	–	–	1.13 (0.60–2.11)	0.708	–	–
PLR >150	0.88 (0.58–1.33)	0.53	–	–	0.92 (0.54–1.58)	0.765	–	–
BLR >0.94	1.84 (1.17–2.88)	0.008*	2.01 (1.27–3.18)	0.003*	1.70 (0.96–3.00)	0.067	1.87 (1.04–3.37)	0.04*
SLR >0.72	1.04 (0.61–1.77)	0.88	–	–	0.79 (0.42–1.48)	0.459	–	–
tMTV >105 mL	1.95 (1.21–3.15)	0.006*	–	–	2.32 (1.31–4.13)	0.004*	2.16 (1.20–3.90)	0.01*
wbTLG >219 g	2.01 (1.29–3.14)	0.002*	2.00 (1.28–3.12)	0.002*	1.77 (0.99–3.14)	0.053	–	–

*, P<0.05. PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; FDG, fluorodeoxyglucose; dNLR, derived neutrophil-to-lymphocyte ratio; SII, systemic immune inflammation index; PLR, platelet-to-lymphocyte ratio; BLR, bone marrow to liver ratio; SLR, spleen to liver ratio; tMTV, total metabolic tumor volume; wbTLG, whole-body total lesion glycolysis.

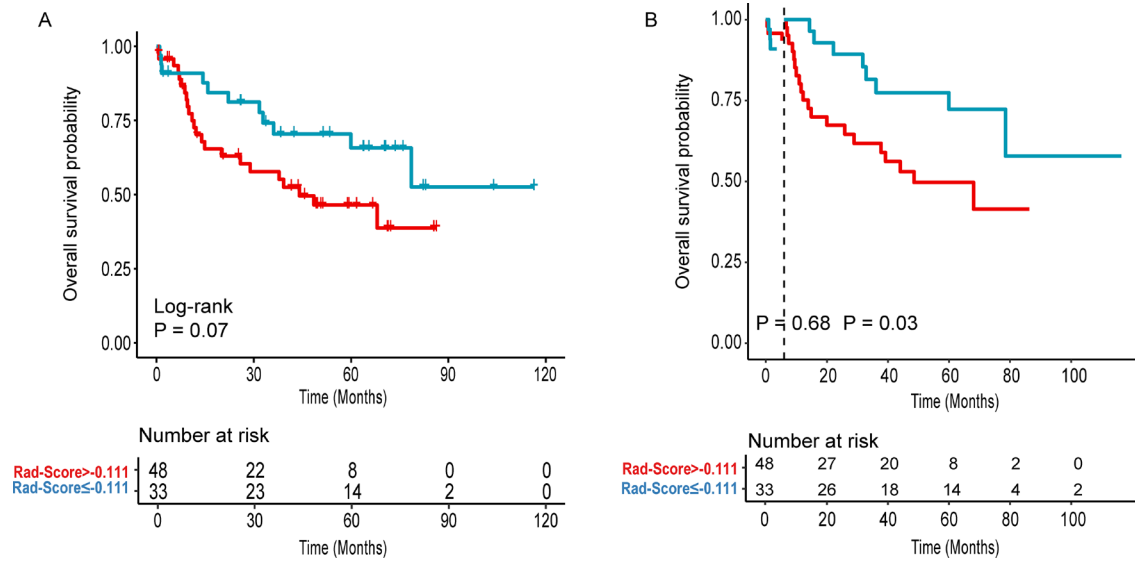


Figure S2 The survival curves for OS between patients with high and low Rad-score. (A) The Kaplan-Meier survival curves and (B) landmark analysis between patients with Rad-score >-0.111 and Rad-score ≤-0.111 for OS in Cohort B. Rad-score, radiomics score; OS, overall survival.

Table S4 The area under time-dependent receiver-operating characteristic curves based on Metabolic, Radiomics, and Radiomicsmetabolic models for PFS

Months	Metabolic		Radiomics		Radiomicsmetabolic	
	AUC (95% CI)	P value [†]	AUC (95% CI)	P value [†]	AUC (95% CI)	P value
6	0.639 (0.534–0.744)	0.04*	0.594 (0.530–0.659)	0.055	0.687 (0.590–0.783)	Ref.
9	0.752 (0.663–0.841)	0.04*	0.617 (0.546–0.687)	<0.001*	0.794 (0.710–0.878)	Ref.
12	0.757 (0.667–0.848)	0.03*	0.649 (0.568–0.730)	<0.001*	0.814 (0.729–0.898)	Ref.
24	0.775 (0.672–0.879)	0.13	0.679 (0.538–0.821)	0.002*	0.843 (0.740–0.946)	Ref.

[†], Delong test results between the Radiomicsmetabolic and Radiomics/Metabolic models. *, $P < 0.05$. HR, hazard ratio; CI, confidence interval; PFS, progression-free survival; AUC, area under the curve; Ref., reference.

Table S5 Multivariate Cox regression analysis for the Radiomicsmetabolic and Radiomicsmetabolicos models adjusting for confounders

Parameters	Radiomicsmetabolic [†]		Radiomicsmetabolicos [†]	
	HR (95% CI)	P value	HR (95% CI)	P value
Histology (squamous cell)	1.588 (0.986–2.556)	0.06	1.641 (0.900–2.992)	0.11
Liver metastases (yes)	3.169 (1.542–6.516)	0.002*	3.496 (1.435–8.517)	0.006*
BLR (>0.94)	1.780 (1.096–2.891)	0.02*	1.885 (1.013–3.507)	0.045*
wbTLG (>219 g)	2.109 (1.308–3.400)	0.002*		
tMTV (>105 mL)			2.162 (1.134–4.119)	0.02*
Rad-score for PFS (>0.093)	3.210 (1.573–6.551)	0.001*		
Rad-score for OS (>0.705)			2.455 (1.324–4.550)	0.004*

[†], adjusting for the stage, immunotherapy line and combination regimen. *, P<0.05. HR, hazard ratio; CI, confidence interval; BLR, bone marrow to liver ratio; wbTLG, whole-body total lesion glycolysis; tMTV, total metabolic tumor volume; Rad-score, radiomics score; PFS, progression-free survival; OS, overall survival.

Table S6 The area under time-dependent receiver-operating characteristic curves based on Metabolicos, Radiomicos, and Radiomicsmetabolicos models for OS

Year(s)	Metabolicos		Radiomicos		Radiomicsmetabolicos	
	AUC (95% CI)	P value [†]	AUC (95% CI)	P value [†]	AUC (95% CI)	P value
0.5	0.757 (0.619–0.895)	0.45	0.591 (0.456–0.726)	0.009*	0.786 (0.637–0.936)	Ref.
1	0.605 (0.487–0.723)	0.049*	0.620 (0.519–0.721)	0.14	0.687 (0.566–0.809)	Ref.
2	0.707 (0.586–0.828)	0.70	0.562 (0.442–0.682)	0.002*	0.728 (0.611–0.844)	Ref.
3	0.770 (0.625–0.916)	0.33	0.664 (0.503–0.822)	0.008*	0.837 (0.735–0.939)	Ref.

[†], Delong test results between the Radiomicsmetabolicos and Metabolicos/Radiomicos models. *, P<0.05. OS, overall survival; AUC, area under the curve; CI, confidence interval; Ref., reference.

Table S7 List of DEGs between two Rad-score groups for OS by DESeq

Genes	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>LGALS4</i>	82.36097	3.633170197	0.514617	7.059948	<0.001	<0.001
<i>UGT2B7</i>	8.963503	3.606238985	0.586421	6.149573	<0.001	<0.001
<i>ARL14</i>	17.94693	3.620928367	0.600929	6.025556	<0.001	<0.001
<i>ANXA10</i>	26.13846	2.817565389	0.477854	5.896287	<0.001	<0.001
<i>CALCA</i>	45.31942	-3.949280052	0.667028	-5.92071	<0.001	<0.001
<i>KRT23</i>	50.96621	2.927060688	0.49764	5.881883	<0.001	<0.001
<i>LOC105373116</i>	18.40357	-4.150745545	0.696693	-5.95778	<0.001	<0.001
<i>OLFM4</i>	70.22448	4.768462286	0.816588	5.839495	<0.001	<0.001
<i>SERPINA3</i>	420.5457	2.367344902	0.431324	5.488554	<0.001	<0.001
<i>ANKS4B</i>	16.9267	3.407518642	0.64832	5.255917	<0.001	<0.001
<i>HMGCS2</i>	23.45541	3.336387806	0.646027	5.164475	<0.001	<0.001
<i>KLK12</i>	10.66841	-3.157199687	0.622605	-5.07095	<0.001	<0.001
<i>MTRNR2L1</i>	216.9609	2.499234205	0.509422	4.906019	<0.001	0.002
<i>ZMAT4</i>	13.57845	-2.99568683	0.609182	-4.91755	<0.001	0.002
<i>CDH17</i>	53.81299	2.447295273	0.51369	4.764151	<0.001	0.002
<i>GOLGA2P6</i>	7.512187	-2.061479747	0.438327	-4.70306	<0.001	0.003
<i>CNTNAP2</i>	77.14768	2.150806035	0.459612	4.679613	<0.001	0.003
<i>SYT8</i>	66.11388	2.128259795	0.460591	4.620719	<0.001	0.003
<i>AQP5</i>	221.6542	2.917240936	0.638306	4.570287	<0.001	0.004
<i>MAGEC1</i>	4.664417	-4.281476683	0.960841	-4.45597	<0.001	0.006
<i>TFF1</i>	8.018441	3.707678287	0.834408	4.443482	<0.001	0.006
<i>CLDN8</i>	34.69863	-2.365552446	0.533608	-4.43312	<0.001	0.006
<i>CPS1</i>	252.4592	2.208255549	0.499878	4.41759	<0.001	0.006
<i>CRLF1</i>	253.957	-2.158560813	0.490018	-4.40507	<0.001	0.006
<i>PAEP</i>	28.05508	-2.780882604	0.631204	-4.40568	<0.001	0.006
<i>ABCC2</i>	198.5857	2.079842729	0.472936	4.397729	<0.001	0.007
<i>KRT20</i>	11.72347	2.706397659	0.625566	4.326318	<0.001	0.008
<i>MRGPRX3</i>	1.713525	-2.760147481	0.637983	-4.32636	<0.001	0.008
<i>LINC01885</i>	1.904947	-3.256923895	0.7543	-4.31781	<0.001	0.008
<i>AGTR2</i>	42.5746	2.216435495	0.519584	4.265786	<0.001	0.01
<i>MYBPC1</i>	10.69639	2.700907676	0.636274	4.244881	<0.001	0.01
<i>HNF4A</i>	27.65145	2.786685822	0.657313	4.239511	<0.001	0.01
<i>ADH7</i>	37.81573	2.728114228	0.646956	4.216848	<0.001	0.01
<i>AZU1</i>	3.55007	-2.062580362	0.492206	-4.19048	<0.001	0.01
<i>LOC105378150</i>	17.88901	-2.000481859	0.483172	-4.14031	<0.001	0.01

Table S7 (continued)

Table S7 (continued)

Genes	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>CDH12</i>	7.16546	-2.59711387	0.628525	-4.13207	<0.001	0.01
<i>CALML5</i>	13.85165	4.239474751	1.030692	4.113233	<0.001	0.01
<i>SLC14A2-AS1</i>	18.61261	-2.065607417	0.508744	-4.06021	<0.001	0.02
<i>LINC00871</i>	1.96463	-3.136557226	0.78048	-4.01876	<0.001	0.02
<i>LINC02506</i>	4.776018	3.471420987	0.863842	4.018585	<0.001	0.02
<i>LOC101928608</i>	1.42303	-3.284138772	0.82791	-3.96678	<0.001	0.02
<i>TGM5</i>	7.832733	2.313517567	0.584468	3.958332	<0.001	0.02
<i>PSCA</i>	39.26236	2.076191054	0.525879	3.948039	<0.001	0.02
<i>LOC100507560</i>	2.103197	-3.16776478	0.812029	-3.90105	<0.001	0.02
<i>TPH2</i>	1.465462	-2.421035402	0.623518	-3.88287	<0.001	0.02
<i>LINC02515</i>	7.258915	-2.099920276	0.545214	-3.85156	<0.001	0.03
<i>LOC105370436</i>	3.169349	-2.171328797	0.571683	-3.79814	<0.001	0.03
<i>LOC105374051</i>	4.650716	-2.039797383	0.542224	-3.76191	<0.001	0.03
<i>GJB6</i>	60.06038	2.253900522	0.603825	3.732702	<0.001	0.03
<i>DGAT2L6</i>	2.673042	-2.073827472	0.557388	-3.72062	<0.001	0.03
<i>IGHV3-16</i>	14.37437	2.018860035	0.54436	3.708686	<0.001	0.04
<i>LOC107986620</i>	3.633854	-2.48483034	0.673058	-3.69185	<0.001	0.04
<i>C9</i>	2.869266	2.22994222	0.605498	3.682822	<0.001	0.04
<i>DDX53</i>	21.24595	-2.19420191	0.59615	-3.68062	<0.001	0.04
<i>GSTA7P</i>	2.480032	-2.506062887	0.685879	-3.6538	<0.001	0.04
<i>TSG1</i>	1.734761	-2.558473594	0.704605	-3.63107	<0.001	0.04
<i>FGB</i>	97.95208	3.207691945	0.885105	3.624082	<0.001	0.04
<i>TRDN</i>	8.411359	-2.645031619	0.732778	-3.60959	<0.001	0.04
<i>LOC105378340</i>	1.556588	-2.449550942	0.679167	-3.6067	<0.001	0.04
<i>CLCA4</i>	16.97676	2.132944467	0.599579	3.557403	<0.001	0.049

DEG, differentially expressed gene; Rad-score, radiomics score; OS, overall survival.

Table S8 Wilcoxon signed rank test for immune infiltration between two Rad-score groups by TIMER, CIBERSORT, CIBERSORT abs, quanTIseq, xCell, MCP-counter and EPIC algorithms

Cell type	Rad-score >0.093 vs. ≤0.093, P value	
	PFS	OS
B_cell_TIMER	0.07	0.23
T_cell_CD4_TIMER	0.56	0.89
T_cell_CD8_TIMER	0.30	0.10
Neutrophil_TIMER	0.007*	0.13
Macrophage_TIMER	0.03*	0.14
Myeloid_dendritic_cell_TIMER	0.89	0.79
B_cell_naive_CIBERSORT	0.61	0.89
B_cell_memory_CIBERSORT	0.15	0.76
B_cell_plasma_CIBERSORT	0.25	0.74
T_cell_CD8_CIBERSORT	0.62	0.63
T_cell_CD4_naive_CIBERSORT	0.43	0.39
T_cell_CD4_memory_resting_CIBERSORT	0.55	0.66
T_cell_CD4_memory_activated_CIBERSORT	0.78	0.39
T_cell_follicular_helper_CIBERSORT	0.54	0.30
T_cell_regulatory_Tregs_CIBERSORT	0.41	0.01*
T_cell_gamma_delta_CIBERSORT	0.32	0.33
NK_cell_resting_CIBERSORT	0.90	0.08
NK_cell_activated_CIBERSORT	0.85	0.96
Monocyte_CIBERSORT	0.62	0.21
Macrophage_M0_CIBERSORT	0.60	0.97
Macrophage_M1_CIBERSORT	0.90	0.44
Macrophage_M2_CIBERSORT	0.38	0.51
Myeloid_dendritic_cell_resting_CIBERSORT	0.58	0.87
Myeloid_dendritic_cell_activated_CIBERSORT	0.88	0.55
Mast_cell_activated_CIBERSORT	0.65	0.35
Mast_cell_resting_CIBERSORT	0.59	0.26
Eosinophil_CIBERSORT	0.62	0.59
Neutrophil_CIBERSORT	0.73	0.17
B_cell_naive_CIBERSORT.ABS	0.79	0.71
B_cell_memory_CIBERSORT.ABS	0.23	0.94
B_cell_plasma_CIBERSORT.ABS	0.19	0.21
T_cell_CD8_CIBERSORT.ABS	0.45	0.49
T_cell_CD4_naive_CIBERSORT.ABS	0.41	0.41

Table S8 (continued)

Table S8 (continued)

Cell type	Rad-score >0.093 vs. ≤0.093, P value	
	PFS	OS
T_cell_CD4._memory_resting_CIBERSORT.ABS	0.59	0.17
T_cell_CD4._memory_activated_CIBERSORT.ABS	0.90	0.32
T_cell_follicular_helper_CIBERSORT.ABS	0.47	0.34
T_cell_regulatory_.Tregs._CIBERSORT.ABS	0.39	0.01*
T_cell_gamma_delta_CIBERSORT.ABS	0.35	0.34
NK_cell_resting_CIBERSORT.ABS	0.97	0.15
NK_cell_activated_CIBERSORT.ABS	0.92	0.97
Monocyte_CIBERSORT.ABS	0.60	0.15
Macrophage_M0_CIBERSORT.ABS	0.23	0.49
Macrophage_M1_CIBERSORT.ABS	0.79	0.94
Macrophage_M2_CIBERSORT.ABS	0.055	0.047*
Myeloid_dendritic_cell_resting_CIBERSORT.ABS	0.84	0.95
Myeloid_dendritic_cell_activated_CIBERSORT.ABS	0.86	0.96
Mast_cell_activated_CIBERSORT.ABS	0.63	0.20
Mast_cell_resting_CIBERSORT.ABS	0.59	0.26
Eosinophil_CIBERSORT.ABS	0.45	0.69
Neutrophil_CIBERSORT.ABS	0.86	0.35
B_cell_QUANTISEQ	0.52	0.56
Macrophage_M1_QUANTISEQ	0.97	0.63
Macrophage_M2_QUANTISEQ	0.91	0.23
Monocyte_QUANTISEQ	0.41	0.41
Neutrophil_QUANTISEQ	0.76	0.68
T_cell_CD4._.non.regulatory._QUANTISEQ	0.89	0.29
T_cell_CD8._QUANTISEQ	0.79	0.84
T_cell_regulatory_.Tregs._QUANTISEQ	0.13	0.16
Myeloid_dendritic_cell_QUANTISEQ	0.30	0.77
uncharacterized_cell_QUANTISEQ	0.55	0.19
Myeloid_dendritic_cell_activated_XCELL	0.25	0.77
B_cell_XCELL	0.33	0.79
T_cell_CD4._memory_XCELL	0.84	0.67
T_cell_CD4._naive_XCELL	0.77	0.38
T_cell_CD4._.non.regulatory._XCELL	0.50	0.62
T_cell_CD4._central_memory_XCELL	0.86	0.23

Table S8 (continued)

Table S8 (continued)

Cell type	Rad-score >0.093 vs. ≤0.093, P value	
	PFS	OS
T_cell_CD4_effector_memory_XCELL	0.03*	0.81
T_cell_CD8_naive_XCELL	0.99	0.38
T_cell_CD8_XCELL	0.70	0.81
T_cell_CD8_central_memory_XCELL	0.18	0.67
T_cell_CD8_effector_memory_XCELL	0.98	0.68
Class.switched_memory_B_cell_XCELL	0.50	0.98
Common_lymphoid_progenitor_XCELL	0.42	0.64
Common_myeloid_progenitor_XCELL	0.08	0.22
Myeloid_dendritic_cell_XCELL	0.24	0.62
Endothelial_cell_XCELL	0.95	0.70
Eosinophil_XCELL	0.55	0.41
Cancer_associated_fibroblast_XCELL	0.76	0.89
Granulocyte.monocyte_progenitor_XCELL	0.27	0.67
Hematopoietic_stem_cell_XCELL	0.33	0.51
Macrophage_XCELL	0.78	0.72
Macrophage_M1_XCELL	0.41	0.94
Macrophage_M2_XCELL	0.83	0.96
Mast_cell_XCELL	0.53	0.94
B_cell_memory_XCELL	0.02*	0.18
Monocyte_XCELL	0.86	>0.99
B_cell_naive_XCELL	0.85	0.72
Neutrophil_XCELL	0.39	0.86
NK_cell_XCELL	0.65	0.65
T_cell_NK_XCELL	0.40	0.35
Plasmacytoid_dendritic_cell_XCELL	0.62	0.38
B_cell_plasma_XCELL	0.02*	0.47
T_cell_gamma_delta_XCELL	0.65	0.31
T_cell_CD4_Th1_XCELL	0.32	0.46
T_cell_CD4_Th2_XCELL	0.96	0.54
T_cell_regulatory_Tregs_XCELL	0.37	0.11
immune_score_XCELL	0.29	0.92
stroma_score_XCELL	0.72	0.73
microenvironment_score_XCELL	0.31	0.97

Table S8 (continued)

Table S8 (continued)

Cell type	Rad-score >0.093 vs. ≤0.093, P value	
	PFS	OS
B_cell_EPIC	0.17	0.89
Cancer_associated_fibroblast_EPIC	0.09	0.47
T_cell_CD4_EPIC	0.21	0.43
T_cell_CD8_EPIC	0.55	0.65
Endothelial_cell_EPIC	0.69	0.50
Macrophage_EPIC	0.62	0.83
NK_cell_EPIC	0.28	0.44
uncharacterized_cell_EPIC	0.19	0.50
T_cell_MCPCOUNTER	0.21	0.16
T_cell_CD8_MCPCOUNTER	0.25	0.73
cytotoxicity_score_MCPCOUNTER	0.27	0.34
NK_cell_MCPCOUNTER	0.11	0.22
B_cell_MCPCOUNTER	0.91	0.52
Monocyte_MCPCOUNTER	0.32	0.35
Macrophage.Monocyte_MCPCOUNTER	0.32	0.35
Myeloid_dendritic_cell_MCPCOUNTER	0.65	0.47
Neutrophil_MCPCOUNTER	0.73	0.13
Endothelial_cell_MCPCOUNTER	0.24	0.25
Cancer_associated_fibroblast_MCPCOUNTER	0.03*	0.36

*, P<0.05. Rad-score, radiomics score.

Table S9 List of DEGs between two Rad-score groups for PFS by DESeq

Gene	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>KRT5</i>	3,061.546	-6.76331	0.964607	-7.01147	<0.001	<0.001
<i>DSG3</i>	689.6619	-7.62184	1.186218	-6.42533	<0.001	<0.001
<i>PTHLH</i>	317.9853	-5.11223	0.812577	-6.29138	<0.001	<0.001
<i>CALML3</i>	79.01373	-7.99117	1.293084	-6.17993	<0.001	<0.001
<i>NTS</i>	240.5706	-6.43272	1.066129	-6.03372	<0.001	<0.001
<i>DSC3</i>	504.8622	-5.31165	0.887139	-5.98739	<0.001	<0.001
<i>LOC107984198</i>	63.22247	-5.61422	1.034588	-5.42653	<0.001	<0.001
<i>HMGA2-AS1</i>	104.0561	-2.98035	0.578704	-5.15005	<0.001	<0.001
<i>KRT14</i>	200.8834	-5.71448	1.111329	-5.14202	<0.001	<0.001
<i>PADI3</i>	48.09748	-5.31846	1.028238	-5.1724	<0.001	<0.001
<i>PIK3C2G</i>	58.15169	-3.34157	0.644936	-5.18124	<0.001	<0.001
<i>UGT1A8</i>	32.75834	-5.03316	0.96536	-5.21376	<0.001	<0.001
<i>TENM2</i>	103.9726	-3.62859	0.711311	-5.10126	<0.001	<0.001
<i>UGT1A10</i>	58.03844	-5.53148	1.084841	-5.09888	<0.001	<0.001
<i>UPK1B</i>	99.8846	-4.52267	0.885782	-5.10585	<0.001	<0.001
<i>LOC100286922</i>	10.43557	-5.34144	1.054073	-5.06743	<0.001	<0.001
<i>CLCA2</i>	690.0541	-5.02004	0.99703	-5.03499	<0.001	<0.001
<i>UGT1A4</i>	40.81205	-5.26529	1.041906	-5.05352	<0.001	<0.001
<i>UGT1A9</i>	33.21112	-5.24519	1.04222	-5.03271	<0.001	<0.001
<i>UGT1A3</i>	40.76576	-5.12579	1.025062	-5.00047	<0.001	<0.001
<i>SPEG</i>	138.0369	-2.0316	0.409277	-4.96387	<0.001	<0.001
<i>UGT1A1</i>	38.49863	-5.31579	1.072734	-4.95537	<0.001	<0.001
<i>UGT1A6</i>	96.45446	-4.43544	0.897807	-4.9403	<0.001	<0.001
<i>UGT1A5</i>	43.00746	-5.20836	1.063212	-4.89871	<0.001	0.001
<i>IGF2BP2-AS1</i>	23.35665	-2.42648	0.497256	-4.87974	<0.001	0.001
<i>CERNA2</i>	23.72468	-5.50654	1.140313	-4.82897	<0.001	0.001
<i>LINC01116</i>	13.24243	-2.86102	0.593828	-4.81793	<0.001	0.001
<i>SPOCK1</i>	136.5263	-2.61444	0.551028	-4.74465	<0.001	0.002
<i>CALML3-AS1</i>	28.83906	-4.00566	0.845733	-4.73632	<0.001	0.002
<i>PTPRZ1</i>	442.1216	-3.34018	0.712032	-4.69105	<0.001	0.002
<i>KRT13</i>	69.44323	-4.3489	0.933512	-4.65864	<0.001	0.003
<i>DNAJB3</i>	15.27441	-4.96217	1.070693	-4.63454	<0.001	0.003
<i>CALCA</i>	60.19364	-4.74083	1.026799	-4.6171	<0.001	0.003
<i>GNG4</i>	41.69476	-3.30015	0.723547	-4.56107	<0.001	0.003
<i>INSL4</i>	3.063367	5.394295	1.181772	4.564581	<0.001	0.003

Table S9 (continued)

Table S9 (continued)

Gene	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>LOC101928266</i>	16.2381	-2.58229	0.566603	-4.55751	<0.001	0.003
<i>LOC105370850</i>	20.86249	2.861851	0.62487	4.579914	<0.001	0.003
<i>LOC105376850</i>	3.997057	-3.42527	0.750354	-4.56487	<0.001	0.003
<i>LOC107985962</i>	116.2388	-4.16807	0.91069	-4.57682	<0.001	0.003
<i>MMP1</i>	624.0417	-2.98373	0.65435	-4.55985	<0.001	0.003
<i>LOC105373893</i>	5.394843	-3.42816	0.753691	-4.5485	<0.001	0.003
<i>HOXA13</i>	14.72076	-5.1056	1.135509	-4.49631	<0.001	0.004
<i>MMP10</i>	234.5878	-3.91214	0.875287	-4.46955	<0.001	0.004
<i>ACTG1P25</i>	4.988968	-2.26335	0.509195	-4.44496	<0.001	0.005
<i>CHGA</i>	23.61473	-3.46198	0.780657	-4.43471	<0.001	0.005
<i>DYNC111</i>	54.38026	-2.14783	0.484966	-4.42883	<0.001	0.005
<i>MAPK4</i>	32.38348	2.594276	0.585858	4.428169	<0.001	0.005
<i>DLX6-AS1</i>	14.17745	-4.10521	0.932588	-4.40196	<0.001	0.006
<i>MMP11</i>	482.3946	-2.4466	0.558653	-4.37948	<0.001	0.006
<i>RAB3B</i>	94.61342	-2.68929	0.614011	-4.37987	<0.001	0.006
<i>SERPINB2</i>	33.67876	-3.79846	0.873064	-4.35072	<0.001	0.006
<i>LOC102724938</i>	18.77664	2.661815	0.613522	4.338578	<0.001	0.007
<i>POTEE</i>	85.25239	-3.45058	0.799517	-4.31582	<0.001	0.007
<i>SERPINB13</i>	67.4718	-5.0954	1.17903	-4.32169	<0.001	0.007
<i>MRAP2</i>	25.63664	-2.28478	0.5299	-4.31172	<0.001	0.007
<i>LOC105373890</i>	2.222073	-3.29076	0.764279	-4.3057	<0.001	0.007
<i>WTAPP1</i>	105.005	-2.5609	0.595292	-4.30193	<0.001	0.007
<i>MPPED2</i>	24.13965	-2.48985	0.580633	-4.28817	<0.001	0.007
<i>CEL</i>	32.67909	-2.46784	0.578126	-4.26868	<0.001	0.008
<i>IVL</i>	53.62137	-3.76857	0.884982	-4.25835	<0.001	0.008
<i>BNC1</i>	104.6002	-3.95034	0.929433	-4.25027	<0.001	0.008
<i>NRCAM</i>	275.4371	-2.20814	0.522109	-4.22928	<0.001	0.009
<i>SLC5A12</i>	18.0428	-3.19011	0.754059	-4.23058	<0.001	0.009
<i>OLFM4</i>	70.22448	-5.02641	1.194279	-4.20874	<0.001	0.009
<i>HAP1</i>	18.84031	-2.78883	0.663567	-4.20278	<0.001	0.009
<i>LOC105369143</i>	3.617015	-2.96033	0.706303	-4.19131	<0.001	0.01
<i>LOC105369863</i>	15.48494	-2.17896	0.519969	-4.19056	<0.001	0.01
<i>SOX11</i>	29.0749	-2.78417	0.665547	-4.18327	<0.001	0.01
<i>CDH8</i>	20.48308	-2.82954	0.676927	-4.17998	<0.001	0.01

Table S9 (continued)

Table S9 (continued)

Gene	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>FOXD1</i>	16.4082	-3.51287	0.843673	-4.16378	<0.001	0.01
<i>LOC101928202</i>	12.42219	2.561813	0.615343	4.163225	<0.001	0.01
<i>ARTN</i>	17.62142	-2.24822	0.541363	-4.15288	<0.001	0.01
<i>SOX21</i>	29.59224	-2.88304	0.696737	-4.13791	<0.001	0.01
<i>TMEM40</i>	24.27937	-2.89614	0.700134	-4.13655	<0.001	0.01
<i>LINC02296</i>	1.864254	-3.24686	0.789122	-4.11453	<0.001	0.01
<i>LOC105370756</i>	5.012	-2.84674	0.695053	-4.09572	<0.001	0.01
<i>SCGB3A1</i>	1268.228	3.184367	0.77802	4.092913	<0.001	0.01
<i>SLC6A15</i>	51.21257	-5.02367	1.230641	-4.08216	<0.001	0.01
<i>LINC02990</i>	7.122855	-2.8335	0.694553	-4.0796	<0.001	0.01
<i>SLC24A2</i>	28.54128	-2.00083	0.490916	-4.07571	<0.001	0.01
<i>RPSAP52</i>	4.389562	-3.49193	0.862081	-4.05058	<0.001	0.01
<i>COL11A1</i>	901.2049	-2.63859	0.654898	-4.02902	<0.001	0.02
<i>UGT1A7</i>	41.61863	-4.41636	1.102888	-4.00436	<0.001	0.02
<i>LINC02253</i>	9.423116	-4.96898	1.242698	-3.99854	<0.001	0.02
<i>NTRK2</i>	349.7008	-2.53871	0.637227	-3.98399	<0.001	0.02
<i>LOC107985088</i>	25.5678	-2.96404	0.74548	-3.97602	<0.001	0.02
<i>HOXB9</i>	14.90799	-4.04478	1.019074	-3.96907	<0.001	0.02
<i>LOC105373873</i>	4.663724	-3.36143	0.846874	-3.96923	<0.001	0.02
<i>HOXD10</i>	24.93047	-3.51409	0.8882	-3.95642	<0.001	0.02
<i>LOC105373754</i>	1.818719	-3.02012	0.764923	-3.94826	<0.001	0.02
<i>LOC105374122</i>	9.950884	-2.71567	0.688608	-3.94371	<0.001	0.02
<i>DUSP9</i>	13.25448	-2.7441	0.698117	-3.93072	<0.001	0.02
<i>MMP13</i>	384.8228	-2.68735	0.684177	-3.92786	<0.001	0.02
<i>LOC105370256</i>	43.85866	-2.96436	0.755208	-3.92523	<0.001	0.02
<i>CDH12</i>	7.041227	-3.91751	0.999668	-3.91881	<0.001	0.02
<i>NEFH</i>	34.12116	-2.37882	0.607651	-3.91478	<0.001	0.02
<i>S100A2</i>	322.4387	-2.81789	0.721728	-3.90436	<0.001	0.02
<i>ULBP2</i>	21.75594	-2.16657	0.558448	-3.87963	<0.001	0.02
<i>HOXC6</i>	19.49047	-2.40807	0.621019	-3.87762	<0.001	0.02
<i>ZMAT4</i>	11.03775	-3.48817	0.901259	-3.87033	<0.001	0.02
<i>CAPNS2</i>	36.91971	-2.7784	0.720014	-3.85882	<0.001	0.02
<i>FAT2</i>	840.2251	-2.71233	0.706262	-3.84041	<0.001	0.02
<i>LINC00958</i>	35.35105	-3.09599	0.805851	-3.84189	<0.001	0.02

Table S9 (continued)

Table S9 (continued)

Gene	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>LINC01305</i>	3.790619	-4.51293	1.174439	-3.84263	<0.001	0.02
<i>ST6GAL2</i>	59.47367	-2.23053	0.580579	-3.84191	<0.001	0.02
<i>DUSP13</i>	6.940374	-4.27147	1.11458	-3.83236	<0.001	0.02
<i>MUC12</i>	15.07699	-2.07873	0.542485	-3.83186	<0.001	0.02
<i>SERPINB11</i>	12.32938	-4.14565	1.080562	-3.83657	<0.001	0.02
<i>LOC107984684</i>	6.41471	-3.15192	0.824124	-3.82457	<0.001	0.02
<i>LYPD6</i>	26.28792	-2.33561	0.613291	-3.80831	<0.001	0.03
<i>LOC105370849</i>	16.62631	2.275119	0.601261	3.783914	<0.001	0.03
<i>LRP1B</i>	38.04372	-2.46171	0.650911	-3.78195	<0.001	0.03
<i>LOC112268302</i>	4.334218	-3.14867	0.833492	-3.77769	<0.001	0.03
<i>GBP6</i>	187.6399	-2.74421	0.73035	-3.75739	<0.001	0.03
<i>LOC105375688</i>	11.92271	-3.96559	1.056227	-3.75448	<0.001	0.03
<i>SHOX2</i>	23.48455	-2.30956	0.614922	-3.75586	<0.001	0.03
<i>SPRR2A</i>	17.94535	-6.09335	1.622605	-3.75529	<0.001	0.03
<i>VSTM5</i>	6.938688	-2.02177	0.538116	-3.75712	<0.001	0.03
<i>IGSF11</i>	18.92674	-2.36678	0.630728	-3.75246	<0.001	0.03
<i>COL4A6</i>	91.60412	-2.376	0.633717	-3.74931	<0.001	0.03
<i>LOC105370852</i>	13.50814	2.377927	0.633987	3.750751	<0.001	0.03
<i>ADCY2</i>	22.23762	-2.09034	0.558262	-3.74437	<0.001	0.03
<i>C12orf56</i>	31.03221	-2.43769	0.650637	-3.74663	<0.001	0.03
<i>LINC01399</i>	6.835195	-2.9595	0.79197	-3.73688	<0.001	0.03
<i>LOC105376611</i>	7.369487	-2.34058	0.626684	-3.73485	<0.001	0.03
<i>LINC02688</i>	4.310668	2.17817	0.58349	3.733006	<0.001	0.03
<i>HOXD13</i>	11.10229	-4.63773	1.24728	-3.71828	<0.001	0.03
<i>LOC105374608</i>	2.786265	-2.72585	0.734132	-3.71302	<0.001	0.03
<i>LOC105377272</i>	3.596491	-3.52709	0.949791	-3.71354	<0.001	0.03
<i>LOC101927025</i>	3.225015	-3.3568	0.905037	-3.70902	<0.001	0.03
<i>MAFA-AS1</i>	2.08046	-3.4515	0.931354	-3.70589	<0.001	0.03
<i>LOC105373895</i>	1.633093	-3.09606	0.837632	-3.69621	<0.001	0.03
<i>MUC3A</i>	64.66161	-2.10511	0.569466	-3.69664	<0.001	0.03
<i>CDHR1</i>	32.24926	-2.5829	0.699171	-3.69424	<0.001	0.03
<i>LOC105376011</i>	7.580907	-3.88509	1.053821	-3.68667	<0.001	0.03
<i>PAX9</i>	119.875	-2.04544	0.555294	-3.68353	<0.001	0.03
<i>FBN2</i>	111.7893	-2.08651	0.567434	-3.6771	<0.001	0.03

Table S9 (continued)

Table S9 (continued)

Gene	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
LINC01206	12.14701	-4.02379	1.096555	-3.66948	<0.001	0.03
LOC107984169	2.501033	-3.44679	0.93939	-3.66918	<0.001	0.03
HOXD9	12.32004	-2.16616	0.591189	-3.66407	<0.001	0.03
LINC01234	6.340233	-4.01354	1.096687	-3.65969	<0.001	0.03
LOC107984376	12.31352	-2.47718	0.676245	-3.66314	<0.001	0.03
SYT14	44.56875	-3.30145	0.902254	-3.65912	<0.001	0.03
LINC01419	5.789775	-4.92364	1.348123	-3.65221	<0.001	0.04
KCNK9	3.781227	-3.39431	0.934792	-3.63109	<0.001	0.04
LINC01117	3.851396	-2.19238	0.603292	-3.63403	<0.001	0.04
LINC01833	12.36984	-3.46982	0.955006	-3.6333	<0.001	0.04
LOC105374154	2.703781	-4.04193	1.112603	-3.63285	<0.001	0.04
TEX55	4.246758	-2.74239	0.75586	-3.62818	<0.001	0.04
FGB	81.46036	-4.31299	1.191714	-3.61914	<0.001	0.04
GOLGA2P11	18.38151	2.223806	0.61491	3.616477	<0.001	0.04
PNCK	38.87082	-2.98469	0.825449	-3.61584	<0.001	0.04
LOC105371307	9.71857	-2.72016	0.753134	-3.61179	<0.001	0.04
CHP2	6.714994	-4.01814	1.112964	-3.6103	<0.001	0.04
LOC105373150	4.535628	-3.62352	1.004607	-3.6069	<0.001	0.04
LOC105378849	5.650864	-3.06574	0.85013	-3.6062	<0.001	0.04
ONECUT2	35.43719	-2.25547	0.625694	-3.60474	<0.001	0.04
ZIC4	8.14779	-4.70037	1.307187	-3.59579	<0.001	0.04
LOC101060400	7.758226	-3.20996	0.895445	-3.58476	<0.001	0.04
MIR4652	3.29045	-3.15309	0.879213	-3.58626	<0.001	0.04
SYT5	4.920904	-2.99298	0.837878	-3.5721	<0.001	0.04
LOC105372036	10.77678	-2.54743	0.713904	-3.56831	<0.001	0.04
RIMS2	117.949	-2.6634	0.748627	-3.55771	<0.001	0.04
KLK10	31.84789	-2.11811	0.595891	-3.55453	<0.001	0.04
LOC107985005	4.244432	-2.37176	0.66716	-3.55501	<0.001	0.04
LINC02893	12.31481	-2.71079	0.764152	-3.54745	<0.001	0.04
DMRT2	15.34216	-2.33985	0.661008	-3.53982	<0.001	0.04
FRMPD2B	7.988492	-2.30144	0.650547	-3.5377	<0.001	0.04
BBOX1	33.58244	-2.02031	0.572034	-3.53181	<0.001	0.04
USH1C	16.2063	-2.45373	0.694599	-3.53258	<0.001	0.04
AOC1	131.5752	-2.27102	0.643338	-3.53006	<0.001	0.04

Table S9 (continued)

Table S9 (continued)

Gene	Base mean	Log ₂ fold change	LfcSE	Stat	P value	P adj
<i>SOX2</i>	198.3139	-2.38111	0.676674	-3.51885	<0.001	0.04
<i>LOC107985634</i>	2.105565	-3.66255	1.043804	-3.50885	<0.001	0.04
<i>LOC107985164</i>	16.20691	-2.92837	0.836583	-3.50039	<0.001	0.046
<i>LINC02348</i>	7.574816	-2.72404	0.779699	-3.4937	<0.001	0.046
<i>NECAB2</i>	3.031213	-2.43796	0.698559	-3.48998	<0.001	0.046
<i>LINC01592</i>	2.598517	-3.7562	1.078667	-3.48226	<0.001	0.046
<i>MYCN</i>	15.90567	-2.04755	0.588918	-3.47679	<0.001	0.047
<i>LOC105371308</i>	18.00957	-2.61753	0.754169	-3.47075	<0.001	0.047
<i>LOC105377609</i>	2.603563	-3.31505	0.95565	-3.4689	<0.001	0.047
<i>NFE4</i>	4.849496	-2.73334	0.787432	-3.47121	<0.001	0.047
<i>PADI1</i>	36.43885	-2.9384	0.846433	-3.47151	<0.001	0.047
<i>CEACAM7</i>	24.04005	-2.66092	0.76883	-3.461	<0.001	0.048
<i>MYRF-AS1</i>	2.68119	-2.65957	0.768254	-3.46184	<0.001	0.048
<i>SPRR1A</i>	23.09538	-4.07158	1.177374	-3.45819	<0.001	0.048
<i>IQCM</i>	2.350245	-3.37275	0.97673	-3.4531	<0.001	0.048

DEG, differentially expressed gene; Rad-score, radiomics score; PFS, progression-free survival.

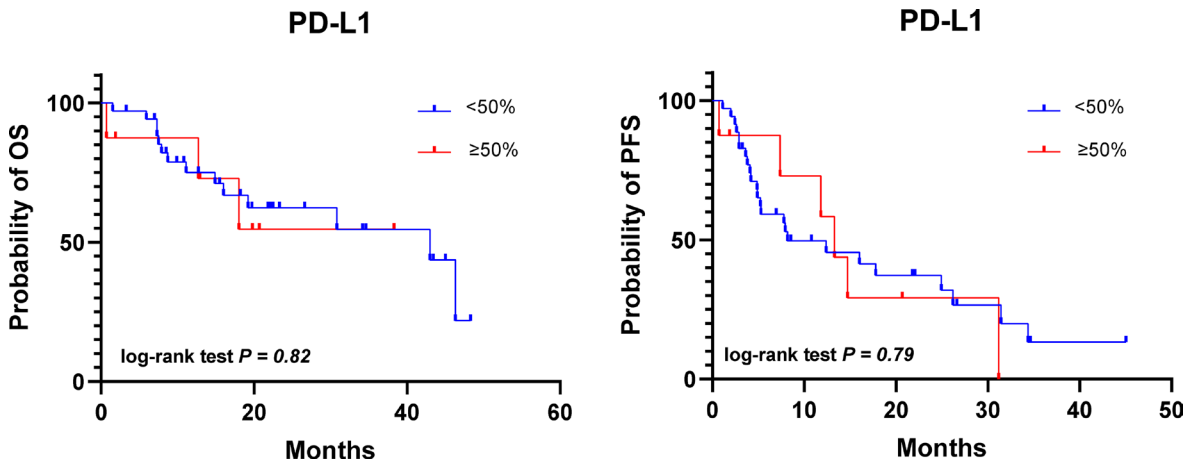


Figure S3 The Kaplan-Meier survival curves between patients with different PD-L1 TPS ($\geq 50\%$ vs. $< 50\%$) levels for OS and PFS. PD-L1, programmed death-ligand 1; OS, overall survival; PFS, progression-free survival.

Table S10 Multivariate analysis of metabolic parameters for OS and PFS in low PD-L1 expression group

Parameters	OS, P value [†]	PFS, P value [†]
PD-L1 _{lo} tMTV _{hi} (vs. PD-L1 _{lo} tMTV _{lo})	0.001*	0.17
PD-L1 _{lo} wbTLG _{hi} (vs. PD-L1 _{lo} wbTLG _{lo})	<0.001*	0.008*
PD-L1 _{lo} BLR _{hi} (vs. PD-L1 _{lo} BLR _{lo})	0.28	0.06

[†], adjusting for the immunotherapy line, combination regimen, and stage. *, $P < 0.05$. OS, overall survival; PFS, progression-free survival; BLR, bone marrow to liver ratio; PD-L1, programmed death-ligand 1; tMTV, total metabolic tumor volume; wbTLG, whole-body total lesion glycolysis.

Table S11 Univariate and multivariate Cox regression analysis of metabolic burden in metastatic NSCLC

Parameters	OS			PFS		
	Univariate	Multivariate		Univariate	Multivariate	
	P value	HR (95% CI) [†]	P value [†]	P value	HR (95% CI) [†]	P value [†]
Distant metastases MTV	0.009*	2.62 (1.06–6.44)	0.04*	0.19	–	–
Distant metastases TLG	0.01*	2.28 (1.01–5.18)	0.048*	0.049*	1.72 (0.92–3.23)	0.09
Lung lesions MTV	0.13	–	–	0.07	–	–
Lung lesions TLG	0.09	–	–	0.05	–	–
Intrathoracic lymph nodes MTV	0.26	–	–	0.03*	2.31 (1.23–4.33)	0.009*
Intrathoracic lymph nodes TLG	0.10	–	–	0.08	–	–

[†], adjusting for immunotherapy line, combination regimen, age, gender, and liver metastases. *, P<0.05. NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval; OS, overall survival; PFS, progression-free survival; MTV, metabolic tumor volume; TLG, total lesion glycolysis.

Table S12 Univariate and multivariate analysis of the number of FDG-avid lesions for OS in the low-tMTV group

Number of FDG-avid lesions	HR (95% CI)	P value
Crude		
<12 months	1.03 (0.96–1.11)	0.23
12 months and above	0.85 (0.73–0.98)	0.03*
Model 1 [†]		
<12 months	1.01 (0.94–1.09)	0.72
12 months and above	0.82 (0.70–0.96)	0.01*
Model 2 [‡]		
<12 months	1.01 (0.93–1.09)	0.83
12 months and above	0.79 (0.65–0.95)	0.02*

[†], adjusting for tMTV. [‡], adjusting for tMTV, liver metastases, histology, BLR, dNLR, stage, immunotherapy line, and combination regimen. *, P<0.05. FDG, fluorodeoxyglucose; OS, overall survival; tMTV, total metabolic tumor volume; HR, hazard ratio; CI, confidence interval; BLR, bone to liver ratio; dNLR, derived neutrophil-to-lymphocyte ratio.

Table S13 Univariate and multivariate analysis of the number of FDG-avid lesions for OS in the high-tMTV group and for PFS in wbTLG subgroups

Number of FDG-avid lesions	OS		PFS			
	High-tMTV		High-wbTLG		Low-wbTLG	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Crude	1.00 (0.98–1.03)	0.81	1.02 (1.00–1.04)	0.045	0.99 (0.89–1.10)	0.83
Model 1 [†]	1.00 (0.98–1.02)	0.97	1.02 (1.00–1.04)	0.06	1.00 (0.99–1.01)	0.83
Model 2 [‡]	0.96 (0.91–1.92)	0.18	1.02 (1.00–1.04)	0.052	0.94 (0.80–1.10)	0.41

[†], adjusting for tMTV in high tMTV group, and for wbTLG in high/low wbTLG groups. [‡], adjusting for tMTV/wbTLG, liver metastases, histology, BLR, dNLR, stage, immunotherapy line, and combination regimen. FDG, fluorodeoxyglucose; OS, overall survival; tMTV, total metabolic tumor volume; PFS, progression-free survival; wbTLG, whole-body total lesion glycolysis; HR, hazard ratio; CI, confidence interval; BLR, bone marrow to liver ratio; dNLR, derived neutrophil-to-lymphocyte ratio.

Table S14 Univariate logistic or Cox regression analysis based on different cut-off values of total metabolic tumor volume

Total metabolic tumor volume	DCB/NDB, P value	PFS, P value	OS, P value
1 st quartile (23 mL)	0.30	0.03*	0.10
Median (48 mL)	0.30	0.004*	0.02*
3 rd quartile (98 mL)	0.041*	0.008*	0.007*
Previously published cut-off value (75 mL)	0.07	0.004*	0.03*
Best cut-off value based on ROC curve for DCB (105 mL)	0.02*	0.006*	0.004*
Best cut-off value based on Kaplan-Meier curve for PFS (41 mL)	0.050	0.002*	0.02*
Best cut-off value based on Kaplan-Meier curve for OS (144 mL)	0.02*	0.02*	<0.001*

*, P<0.05. DCB, durable clinical benefit; NDB, non-durable clinical benefit; PFS, progression-free survival; OS, overall survival; ROC, receiver operating characteristic.