

Supplementary File S2 Content

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Table S1. Demographic characteristics, pre-treatment serum biomarkers and tumor characteristics of non-response group and response group.

	All patients (n=125)	Non-response Group (n = 91)	Response Group (n = 34)	P value
Demographic Characteristics				
Age, median (IQR), y	58.0 (47.0, 68.0)	58.0 (44.0, 68.0)	60.5 (54.5, 68.3)	0.285
Gender				0.608
Male, n (%)	109 (87.2)	78 (85.7)	31 (91.2)	
Female, n (%)	16 (12.8)	13 (14.3)	3 (8.8)	
BMI, mean \pm SD, kg/m ²	22.0 \pm 2.8	21.8 \pm 2.7	22.4 \pm 2.9	0.293
Smoking History				0.502
Yes, n (%)	42 (33.6)	29 (31.9)	13 (38.2)	
No, n (%)	83 (66.4)	62 (68.1)	21 (61.8)	
Drinking History				0.392
Yes, n (%)	44 (35.2)	30 (33.0)	14 (41.2)	
No, n (%)	81 (64.8)	61 (69.0)	20 (58.8)	
HBV Infection History				0.745
Yes, n (%)	78 (62.4)	56 (61.5)	22 (64.7)	
No, n (%)	47 (37.6)	35 (38.5)	12 (35.3)	
HCV Infection History				/
Yes, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
No, n (%)	125 (100.0)	91 (100.0)	34 (100.0)	
Hypertensive History				0.074
Yes, n (%)	37 (29.6)	31 (34.1)	6 (17.6)	
No, n (%)	88 (70.4)	60 (65.9)	28 (82.4)	

Diabetes History				0.821
Yes, n (%)	18 (14.4)	13 (14.3)	5 (14.7)	
No, n (%)	107 (85.6)	78 (85.7)	29 (85.3)	
Heart Disease				0.467
Yes, n (%)	2 (1.6)	1 (1.1)	1 (2.9)	
No, n (%)	123 (98.4)	90 (98.9)	33 (97.1)	
NAFLD History				/
Yes, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
No, n (%)	125 (100.0)	91 (100.0)	34 (0.0)	
Cirrhosis, n (%)				0.160
Yes, n (%)	105 (84.0)	79 (86.8)	26 (76.5)	
No, n (%)	20 (16.0)	12 (13.2)	8 (23.5)	
ECOG-PS				0.701
Grade 0, n (%)	66 (52.8)	49 (53.8)	17 (50.0)	
Grade 1, n (%)	59 (47.2)	42 (46.2)	17 (50.0)	
Pre-treatment Serum Biomarkers				
RBC, median (IQR), 10 ¹² /L	4.1 (3.7, 4.5)	4.1 (3.6, 4.6)	4.2 (3.7, 4.5)	0.954
WBC, median (IQR), 10 ⁹ /L	6.3 (4.9, 8.0)	6.2 (4.9, 7.8)	6.5 (4.8, 8.2)	0.667
Neut, median (IQR), 10 ⁹ /L	4.1 (2.9, 6.0)	4.0 (2.8, 5.8)	4.3 (3.0, 6.3)	0.348
Mono, median (IQR), 10 ⁹ /L	0.6 (0.4, 0.8)	0.6 (0.4, 0.9)	0.6 (0.4, 0.8)	0.933
Lymph, median (IQR), 10 ⁹ /L	1.1 (0.8, 1.7)	1.1 (0.8, 1.8)	1.0 (0.7, 1.5)	0.363
Hb, mean ± SD, g/L	123.0 ± 22.7	122.5 ± 24.4	124.3 ± 17.5	0.663
PLT, median (IQR), 10 ⁹ /L	167.0 (112.5, 252.0)	167.0 (112.0, 261.0)	167.0 (114.0, 243.8)	0.896

PLR, median (IQR)	138.3 (101.4, 219.3)	135.2 (105.6, 213.8)	146.9 (88.1, 262.1)	0.631
NLR, median (IQR)	3.7 (1.9, 5.9)	3.3 (1.9, 5.6)	4.5 (1.9, 6.7)	0.171
LMR, median (IQR)	2.0 (1.3, 3.6)	2.0 (1.3, 3.8)	1.8 (1.2, 3.0)	0.316
PT, median (IQR), s	14.5 (13.6, 15.5)	14.7 (13.5, 15.7)	14.4 (13.6, 15.2)	0.394
FIB, median (IQR), g/L	3.8 (2.9, 5.2)	3.8 (2.8, 5.4)	3.8 (3.0, 5.1)	0.907
APTT, median (IQR), s	39.3 (36.3, 44.0)	39.1 (36.2, 44.7)	39.5 (36.3, 42.7)	0.788
TT, median (IQR), s	17.3 (16.2, 18.4)	17.3 (16.2, 18.5)	17.4 (15.9, 18.1)	0.566
INR, median (IQR)	1.1 (1.0, 1.2)	1.1 (1.0, 1.2)	1.1 (1.0, 1.2)	0.394
D-D, median (IQR), mg/L	1.5 (0.7, 3.2)	1.3 (0.6, 3.2)	1.9 (0.8, 3.4)	0.340
AFP, median (IQR), ng/mL	161.4 (5.5, 3326.5)	205.3 (8.2, 4149.0)	26.9 (3.7, 1680.9)	0.212
CEA, median (IQR), µg/L	2.4 (1.6, 3.6)	2.4 (1.5, 3.5)	2.4 (1.9, 4.1)	0.598
CA19-9, median (IQR), U/mL	19.9 (10.5, 41.9)	19.9 (10.7, 42.8)	19.9 (8.9, 42.9)	0.430
T-BIL, median (IQR), µmol/L	17.0 (11.5, 25.5)	17.0 (11.0, 26.0)	15.5 (12.0, 25.3)	0.912
D-BIL, median (IQR), µmol/L	8.0 (5.5, 13.0)	8.0 (5.0, 13.0)	7.0 (5.8, 14.3)	0.996
I-BIL, median (IQR), µmol/L	8.0 (6.0, 12.0)	8.0 (6.0, 13.0)	8.0 (6.0, 11.0)	0.753
TP, mean ± SD, g/L	69.9 ± 8.4	70.6 ± 8.5	68.2 ± 7.6	0.152
ALB, median (IQR), g/L	34.6 (31.9, 37.6)	34.7 (30.7, 38.3)	34.3 (32.9, 36.5)	0.824
GLOB, median (IQR), g/L	34.1 (29.4, 38.7)	35.4 (29.4, 39.1)	32.4 (29.6, 36.1)	0.148
A/G, mean ± SD	1.0 ± 0.3	1.0 ± 0.3	1.1 ± 0.2	0.151
ALT, median (IQR), U/L	39.0 (25.0, 68.0)	35.0 (24.0, 56.0)	54.5 (29.8, 88.5)	0.010
AST, median (IQR), U/L	57.0 (39.0, 93.0)	54.0 (37.0, 83.0)	68.0 (45.0, 113.5)	0.080
ALP, median (IQR), U/L	182.0 (115.0, 233.5)	180.0 (116.0, 244.0)	200.0 (109.5, 217.8)	0.866
γ-GTP, median (IQR), U/L	182.0 (74.5, 257.5)	159.0 (64.0, 252.0)	203.0 (82.0, 313.3)	0.314

BUN, median (IQR), mmol/L	5.1 (3.8, 6.4)	5.3 (3.8, 6.1)	4.7 (3.9, 7.7)	0.951
SCr, median (IQR), μ mol/L	68.0 (56.5, 78.0)	69.0 (57.0, 78.0)	62.0 (56.0, 76.5)	0.379
K, mean \pm SD, mmol/L	3.9 \pm 0.5	3.9 \pm 0.5	3.7 \pm 0.3	0.044
Na, median (IQR), mmol/L	137.0 (135.0, 139.0)	137.0 (134.0, 139.0)	137.0 (135.0,139.3)	0.503
Cl, median (IQR), mmol/L	102.0 (99.5, 105.0)	102.0 (99.0, 105.0)	102.5 (100.0, 105.3)	0.513
TC, median (IQR), mmol/L	4.3 (3.4, 5.0)	4.4 (3.4, 5.3)	4.1 (3.4, 4.7)	0.297
TG, median (IQR), mmol/L	1.0 (0.7, 1.2)	0.9 (0.7, 1.2)	1.0 (0.8, 1.2)	0.651
HDL, mean \pm SD, mmol/L	0.9 \pm 0.3	0.9 \pm 0.3	0.9 \pm 0.3	0.877
LDL, median (IQR), mmol/L	2.5 (1.9,3.2)	2.5 (1.8, 3.3)	2.5 (1.9, 2.8)	0.598
Tumor Characteristics				
ALBI Score, mean \pm SD	-2.1 \pm 0.5	-2.1 \pm 0.5	-2.2 \pm 0.5	0.849
Child-Pugh Score				0.750
A (5-6 scores), n (%)	80 (64.0)	59 (64.8)	21 (61.8)	
B (7 scores), n (%)	45 (36.0)	32 (35.2)	13 (38.2)	
T Stage				0.404
T1a, n (%)	4 (3.2)	2 (2.2)	2 (5.9)	
T1b, n (%)	10 (8.0)	6 (6.6)	4 (11.8)	
T2, n (%)	28 (22.4)	23 (25.3)	5 (14.7)	
T3, n (%)	40 (32.0)	27 (29.6)	13 (38.2)	
T4, n (%)	43 (34.4)	33 (36.3)	10 (29.4)	
N Stage				0.585
N0, n (%)	76 (60.8)	54 (59.3)	22 (64.7)	
N1, n (%)	49 (39.2)	37 (40.7)	12 (35.3)	

M Stage				0.358
M0, n (%)	107 (85.6)	80 (87.9)	27 (79.4)	
M1, n (%)	18 (14.4)	11 (12.1)	7 (20.6)	
TNM Stage				0.448
IA, n (%)	2 (1.6)	1 (1.1)	1 (2.9)	
IB, n (%)	9 (7.2)	5 (5.5)	4 (11.8)	
II, n (%)	17 (13.6)	14 (15.4)	3 (8.8)	
IIIA, n (%)	21 (16.8)	14 (15.4)	7 (20.6)	
IIIB, n (%)	13 (10.4)	11 (12.1)	2 (5.9)	
IVA, n (%)	45 (36.0)	35 (38.5)	10 (29.4)	
IVB, n (%)	18 (14.4)	11 (12.1)	7 (20.6)	
BCLC Stage				0.172
A, n (%)	12 (9.6)	6 (6.6)	6 (17.6)	
B, n (%)	38 (30.4)	29 (31.9)	9 (26.5)	
C, n (%)	75 (60.0)	56 (61.5)	19 (55.9)	
Tumor Size, median (IQR), mm	6.9 (3.1, 11.1)	6.8 (2.7, 10.5)	7.0 (4.5, 11.2)	0.478
Tumor Number				0.894
Solitary, n (%)	23 (18.4)	17 (18.7)	6 (17.6)	
Multiple, n (%)	102 (81.6)	74 (81.3)	28 (82.4)	
Vascular Invasion, n (%)				0.473
Yes, n (%)	43 (34.4)	33 (36.3)	10 (29.4)	
No, n (%)	82 (65.6)	58 (63.7)	24 (70.6)	
Lymphatic Metastasis, n (%)				0.641

Yes, n (%)	52 (41.6)	39 (42.9)	13 (38.2)	
No, n (%)	73 (58.4)	52 (57.1)	21 (61.8)	
Distant Metastasis, n (%)				0.358
Yes, n (%)	18 (14.4)	11 (12.1)	7 (20.6)	
No, n (%)	107 (85.6)	80 (87.9)	27 (79.4)	

Abbreviation: BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, non-alcohol fatty liver disease; ECOG-PS, Eastern Cooperative Oncology Group performance status; RBC, red blood cell; WBC, white blood cell; Neut, neutrophil; Mono, monocyte; Lymph, lymphocyte; Hb, hemoglobin; PLT, platelets; PLR, platelet lymphocyte ratio; NLR, neutrophil lymphocyte ratio; LMR, lymphocyte monocyte ratio; PT, prothrombin time; FIB, fibrinogen; APTT, activated partial thromboplastin time; TT, thrombin time; INR, international normalized ratio; D-D, d-dimer; AFP, Alpha feto-protein; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; T-BIL, total bilirubin; D-BIL, direct bilirubin; I-BIL, indirect bilirubin; TP, total protein; ALB, albumin; GLOB, globulin; A/G, albumin/globulin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ -GTP, γ -glutamyl transpeptidase; BUN, blood urea nitrogen; Scr, serum creatinine; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ALBI, albumin-bilirubin; TNM, Tumor Node Metastasis; BCLC, Barcelona Clinic Liver Cancer.

Table S2. The best hyperparameters for five machine learning algorithms.

Machine Learning Algorithms	Best Hyperparameters
CART	criterion= 'gini' max_depth=9 min_samples_split=3 random_state=420
AdaBoost	n_estimators=800 random_state=420 learning_rate=1.0
XGBoost	min_child_weight=1 max_depth=15 learning_rate=0.1 gamma=0.0 colsample_bytree=0.3 random_state=420
SVM	gamma=0.2 C=10 kernel='rbf'
RF	n_estimators=500 random_state=420 criterion='gini' max_depth=10

`max_features='auto'`

Abbreviation: CART, classification and regression tree; AdaBoost, adaptive boosting; XGBoost, extreme gradient boosting; RF, random forest; SVM, support vector machine.

Table S3. The confusion matrix for five machine learning algorithms.

Machine Learning Algorithm	Predicted Labels	Real Labels	
		Response	Non-response
CART	Response	6	5
	Non-response	3	23
AdaBoost	Response	6	5
	Non-response	3	23
XGBoost	Response	6	4
	Non-response	3	24
RF	Response	6	2
	Non-response	3	26
SVM	Response	6	2
	Non-response	3	26

Abbreviation: CART, classification and regression tree; AdaBoost, adaptive boosting; XGBoost, extreme gradient boosting; RF, random forest; SVM, support vector machine.

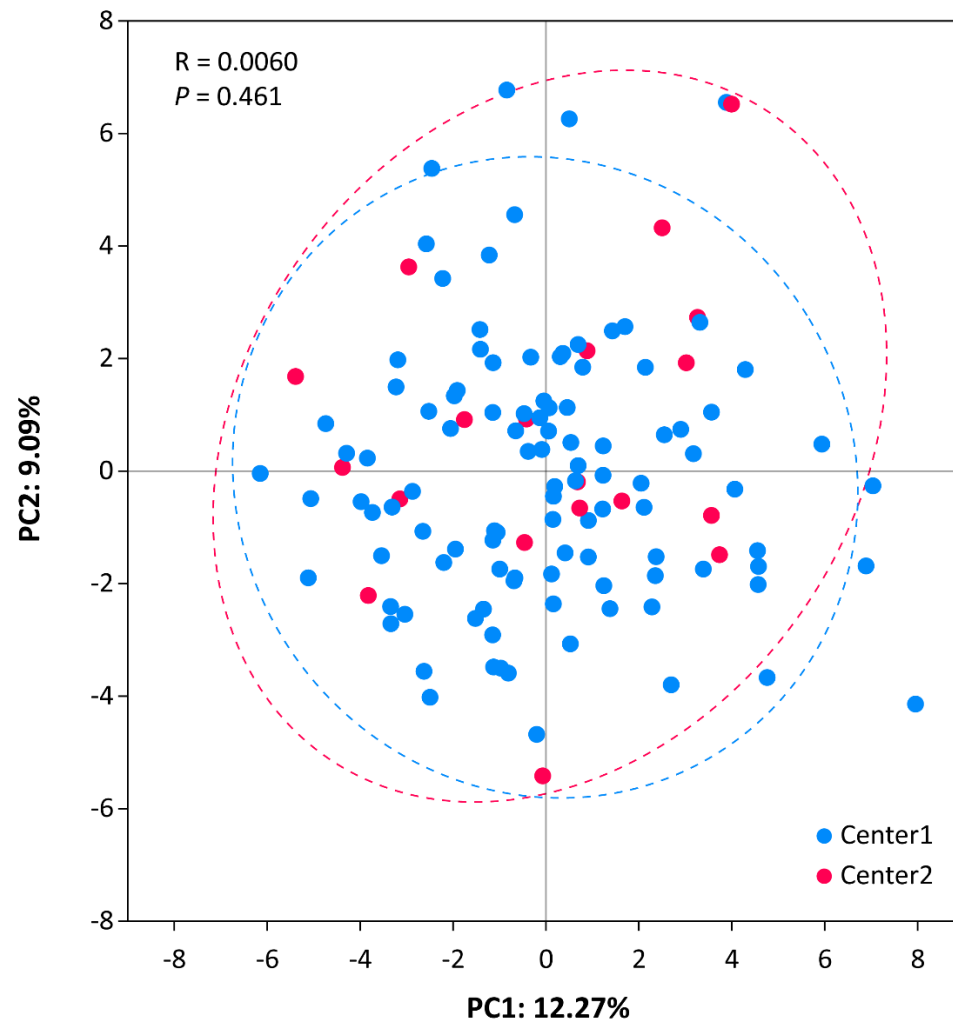


Figure S1. PCA plot of the two medical centers based on 64 standardized clinical features.

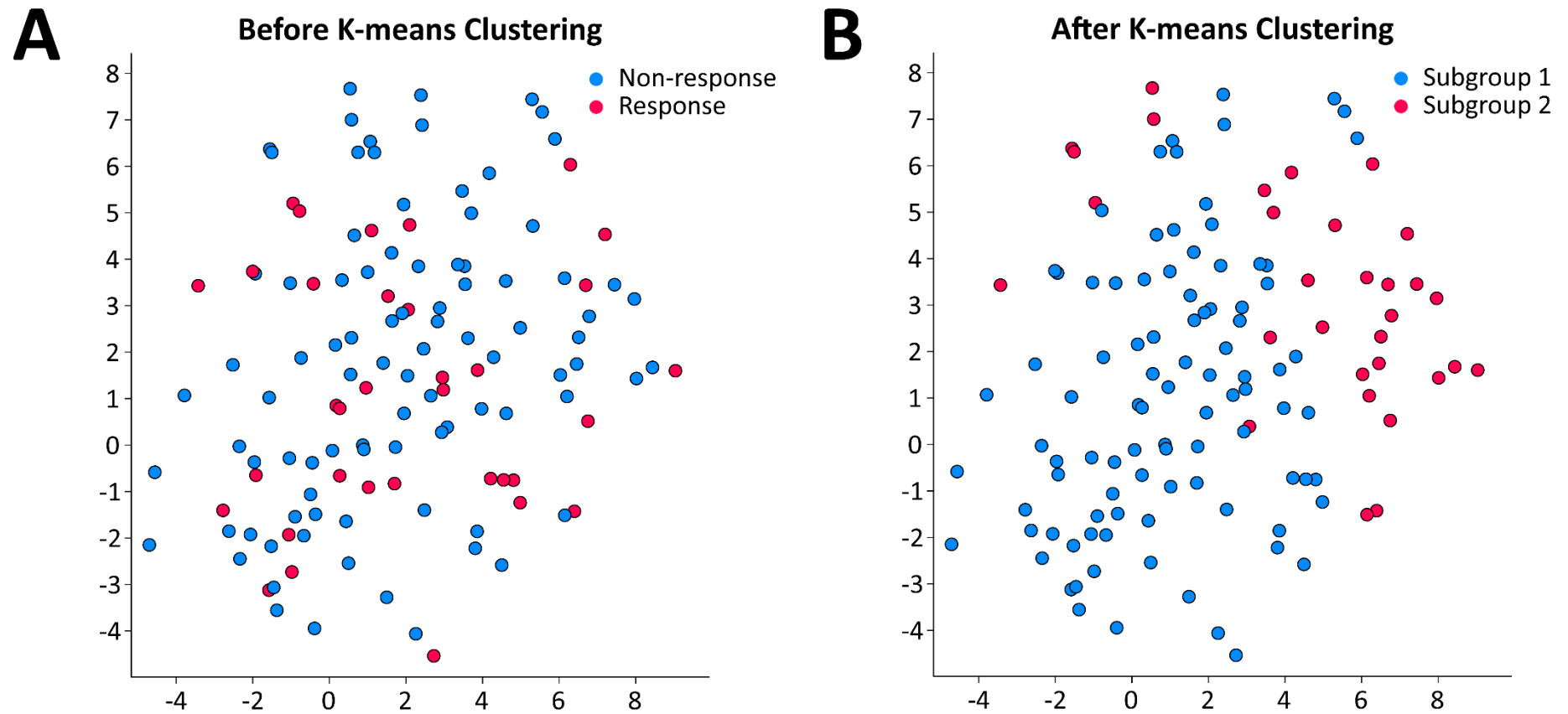


Figure S2. The scatter plot before (A) and after (B) Kmeans clustering.