**Supplementary Table 1. Clinical characteristics of the HCC patients in the four data sets**

# **TCGA training data set, *n* (%)**

**Characteristic**

**Age, years**

# **Number of patients (*n=*250)**

**Low IGSHCC (*n=*125)**

**High IGSHCC (*n=*125)**

***p****-*value

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| <50 | 45 (18) | 18 (14) | 27 (22) | 0.187 |
| ≥50 | 205 (82) | 107 (86) | 98 (78) |  |

Sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Female | 77 (31) | 32 (42) | 45 (58) | 0.100 |
| Male | 173 (69) | 93 (54) | 80 (46) |  |

AFP level, ng/mL

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ≤300 | 147 (20) | 88 (60) | 59 (40) | 0.025 |
| >300 | 37 (20) | 14 (38) | 23 (62) |  |
| Histological grade | | | | |
| G1 & G2 | 159 (64) | 90 (57) | 69 (43) | 0.005 |
| G3 & G4 | 88 (36) | 33 (37.5) | 55 (62.5) |  |
| TNM stage |  |  |  |  |
| I & II | 175 (71) | 95 (54) | 80 (46) | 0.026 |
| III & IV | 73 (29) | 28 (38) | 45 (62) |  |
| Microvascular invasion | | | | |
| No | 143 (67) | 85 (59) | 58 (41) | 0.019 |
| Yes | 70 (33) | 29 (41) | 41 (59) |  |
| TP53 genotype |  |  |  |  |
| Wild-type | 169 (68) | 98 (58) | 71 (42) | <0.001 |
| Mutant  CTNNB1 genotype | 78 (32) | 26 (33) | 52 (67) |  |
| Wild-type | 177 (72) | 84 (47) | 93 (53) | 0.170 |
| Mutant Survival status | 70 (28) | 40 (57) | 30 (43) |  |
| Alive | 157 (63) | 100 (64) | 57 (36) | <0.001 |
| Dead | 93 (27) | 25 (27) | 68 (73) |  |

# **TCGA validation data set**

**Characteristic**

# **Number of patients (*n=*106)**

**Low IGSHCC (*n=*61)**

**High IGSHCC (*n=*45)**

***p-*value**

**Age, years**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| <50 | 21(20) | 11 (52) | 10 (48) | 0.628 |
| ≥50 | 85 (80) | 50 (59) | 35 (41) |  |

Sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Female | 39 (37) | 18 (46) | 21 (54) | 0.103 |
| Male | 67 (63) | 43 (64) | 24 (36) |  |

AFP level, ng/mL

≤300 59 (69) 42 (71) 17 (29) 0.004

>300 27 (31) 10 (37) 17 (63)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Histological grade G1 & G2 | 63 (61) | 42 (67) | 21 (33) | 0.026 |
| G3 & G4 | 41 (39) | 18 (44) | 23 (56) |  |
| TNM stage |  |  |  |  |
| I & II | 73 (69) | 52 (71) | 21 (29) | <0.001 |
| III & IV | 33 (31) | 9 (27) | 24 (73) |  |
| Microvascular invasion | | | | |
| No | 56 (63) | 37 (66) | 19 (34) | 0.121 |
| Yes | 33 (37) | 16 (48.5) | 17 (51.5) |  |
| TP53 genotype |  |  |  |  |
| Wild-type | 61 (58) | 46 (75) | 15 (25) | 0.413 |
| Mutant  CTNNB1 genotype | 44 (42) | 30 (68) | 14 (32) |  |
| Wild-type | 61(58) | 45 (74) | 16 (26) | 0.333 |
| Mutant Survival status | 44 (42) | 36 (82) | 8 (18) |  |
| Alive | 70 (66) | 46 (66) | 24 (34) | 0.023 |
| Dead | 36 (34) | 15 (42) | 21 (58) |  |

# **LCI validation set 1**

**Characteristic**

Age, years

# **Number of patients (*n=*221)**

**Low IGSHCC (*n=*131)**

**High IGSHCC (*n=*90)**

*p-*value

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| <50 | 96 (43) | 54 (56) | 42 (44) | 0.490 |
| ≥50 | 125 (57) | 77 (62) | 48 (38) |  |

Sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Female | 30 (14) | 20 (67) | 10 (33) | 0.428 |
| Male | 191 (86) | 111 (58) | 80 (42) |  |

AFP level, ng/mL

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ≤300 | 118 (54) | 83 (70) | 35 (30) | <0.001 |
| >300 | 100 (46) | 46 (46) | 54 (54) |  |

Tumor size, cm

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ≤5 | 140 (64) | 92 (66) | 48 (34) | 0.010 |
| >5 | 80 (36) | 38 (47.5) | 42 (52.5) |  |

Multinodular

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No | 176 (80) | 109 (62) | 67 (38) | 0.127 |
| Yes BCLC stage | 45 (20) | 22 (49) | 23 (51) |  |
| 0 & A | 168 (77) | 109 (65) | 59 (35) | 0.009 |
| B & C | 51 (23) | 22 (43) | 29 (57) |  |
| TNM stage |  |  |  |  |
| I & II | 170 (78) | 112 (66) | 58 (34) | 0.001 |

III 49 (22) 19 (39) 30 (61)

Survival status

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Alive | 136 (62) | 89 (65) | 47 (35) | 0.024 |
| Dead | 85 (38) | 42 (49) | 43 (51) |  |

# **LCI validation set 2**

**Characteristic**

Age, years

# **Number of patients (*n=*56)**

**Low IGSHCC (*n=*23)**

**High IGSHCC (*n=*33)**

***p-*value**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| <50 | 17 (30) | 5 (29.4) | 12 (70.6) | 0.376 |
| ≥50 | 39 (70) | 18 (46.2) | 21 (53.8) |  |

Sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Female | 5 (9) | 2 (40) | 3 (60) | 1.000 |
| Male | 51 (91) | 21 (41.2) | 30 (58.8) |  |

AFP level, ng/mL

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ≤300 | 41 (73) | 18 (43.9) | 23 (56.1) | 0.551 |
| >300 | 15 (27) | 5 (33.3) | 10 (66.7) |  |

CA19-9 level, U/mL

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ≤36 | 45 (80) | 22 (48.9) | 23 (51.1) | 0.019 |
| >36 | 11 (20) | 1 (9.1) | 10 (90.9) |  |
| Histological grade | | | | |
| G1 & G2 | 34 (61) | 15 (44.1) | 19 (55.9) | 0.592 |
| G3 & G4 | 22 (39) | 8 (36.4) | 14 (63.6) |  |
| BCLC stage |  |  |  |  |
| 0 & A | 30 (54) | 14 (46.7) | 16 (53.3) | 0.422 |
| B & C | 26 (46) | 9 (34.6) | 17 (65.4) |  |
| TNM stage |  |  |  |  |
| I & II | 45 (80) | 21 (46.7) | 24 (53.3) | 0.102 |
| III & IV | 11 (20) | 2 (18.2) | 9 (81.8) |  |
| Microvascular invasion | | | | |
| No | 36 (64) | 15 (41.7) | 21 (58.3) | 1.000 |
| Yes | 20 (36) | 8 (40) | 12 (60) |  |
| HBV DNA level, cps/mL | | | | |
| ≤1000 | 37 (66) | 19 (51.4) | 18 (48.6) | 0.044 |
| >1000  Survival status | 19 (34) | 4 (21.1) | 15 (78.9) |  |
| Alive | 21 (38) | 13 (61.9) | 8 (38.1) | 0.024 |
| Dead | 35 (62) | 10 (28.6) | 25 (71.4) |  |

AFP, -fetoprotein; BCLC, Barcelona Clinic Liver Cancer; HBV, hepatitis B virus. *p-*values were calculated using the Pearson chi-square test.