**Supplementary Table S1 Characteristics of patients in the PSM dataset**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | Patient Cohort (N = 256) | BP ≤ 24m (N = 128) | BP > 24m (N = 128) | *p* |
| Age, n (%) |  |  |  | 0.418 |
| ≤ 65 years | 176(68.8) | 91(71.1) | 85(66.4) |  |
| > 65 years | 80(31.3) | 37(28.9) | 43(33.6) |  |
| Gender, n (%) |  |  |  | 0.375 |
| Female | 149(58.2) | 71(55.5) | 78(60.9) |  |
| Male | 107(41.8) | 57(44.5) | 50(39.1) |  |
| Family history, n (%) |  |  |  | 0.450 |
| No | 224(87.5) | 110(85.9) | 114(89.1) |  |
| Yes | 32(12.5) | 18(14.1) | 14(10.9) |  |
| Smoker, n (%) |  |  |  | 0.877 |
| No | 203(79.3) | 102(79.7) | 101(78.9) |  |
| Yes | 53(20.7) | 26(20.3) | 27(21.1) |  |
| T stage, n (%) |  |  |  | 0.797 |
| T1/T2 | 158(61.7) | 78(60.9) | 80(62.5) |  |
| T3/T4 | 98(38.3) | 50(39.1) | 48(37.5) |  |
| N stage, n (%) |  |  |  | 0.389 |
| N0 | 61(23.8) | 27(21.1) | 34(26.6) |  |
| N1 | 21(8.2) | 8(6.3) | 13(10.2) |  |
| N2 | 113(44.1) | 59(46.1) | 54(42.2) |  |
| N3 | 61(23.8) | 34(26.6) | 27(21.1) |  |
|  |  |  |  |  |
|  |  |  |  |  |

**Continued Supplementary Table S1**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | Patient Cohort (N = 256) | BP ≤ 24m (N = 128) | BP > 24m (N = 128) | *p* |
| Other visceral metastases, n (%) |  |  |  | 0.705 |
| No | 145(56.6) | 71(55.5) | 74(57.8) |  |
| Yes | 111(43.3) | 57(44.5) | 54(42.2) |  |
| Histological type, n (%) |  |  |  | 0.698 |
| ADC | 226(88.3) | 114(89.1) | 112(87.5) |  |
| Other types | 30(11.7) | 14(10.9) | 16(12.5) |  |
| Treatment line, n (%) |  |  |  | 0.452 |
| First-line | 202(78.9) | 105(82.0) | 97(75.8) |  |
| Second-line | 41(16.0) | 17(13.3) | 24(18.8) |  |
| Third-line and above | 13(5.1) | 6(4.7) | 7(5.5) |  |
| BP treatment pattern, n (%) |  |  |  | 0.489 |
| Regular treatment | 73(28.5) | 39(30.5) | 34(26.6) |  |
| Irregular treatment | 183(71.5) | 89(69.5) | 94(73.4) |  |
| Type of BP, n (%) |  |  |  | 1.000 |
| ZOL | 130(50.8) | 65(50.8) | 65(50.8) |  |
| Others | 126(49.2) | 63(49.2) | 63(49.2) |  |

Note: Differences between variables were calculated using the chi-square test. ADC, adenocarcinoma; BP, bisphosphonate; ZOL, zoledronic acid.

**Supplementary Table S2 Characteristics of patients between regular and irregular BP treatment groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | Patient Cohort (N = 359) | Regular treatment (N = 131) | Irregular treatment (N = 228) | *p* |
| Age, median years (IQR) | 61.0(55.0-67.0) | 61.0(54.3-66.8) | 61.0(55.0-67.0) | 0.647 |
| Age, n (%) |  |  |  | 0.751 |
| ≤ 65 years | 253(70.5) | 91(69.5) | 162(71.1) |  |
| > 65 years | 106(29.5) | 40(30.5) | 66(28.9) |  |
| Gender, n (%) |  |  |  | 0.970 |
| Female | 206(57.4) | 75(57.3) | 131(57.5) |  |
| Male | 153(42.6) | 56(42.7) | 97(42.5) |  |
| Family history, n (%) |  |  |  | 0.307 |
| No | 315(87.7) | 118(90.1) | 197(86.4) |  |
| Yes | 44(12.3) | 13(9.9) | 31(13.6) |  |
| Smoker, n (%) |  |  |  | 0.687 |
| No | 289(80.5) | 104(79.4) | 185(81.1) |  |
| Yes | 70(19.5) | 27(20.6) | 43(18.9) |  |
| T stage, n (%) |  |  |  | 0.774 |
| T1/T2 | 220(61.3) | 79(60.3) | 141(61.8) |  |
| T3/T4 | 139(38.7) | 52(39.7) | 87(38.2) |  |
| N stage, n (%) |  |  |  | 0.841 |
| N0 | 88(24.5) | 31(23.7) | 57(25.0) |  |
| N1 | 24(6.7) | 7(5.3) | 17(7.5) |  |
| N2 | 154(42.9) | 59(45.0) | 95(41.7) |  |
| N3 | 93(25.9) | 34(26.0) | 59(25.9) |  |
|  |  |  |  |  |

**Continued Supplementary Table S2**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | Patient Cohort (N = 359) | Regular treatment (N = 131) | Irregular treatment (N = 228) | *p* |
| Other visceral metastases, n (%) |  |  |  | 0.987 |
| No | 203(56.6) | 74(56.5) | 129(56.6) |  |
| Yes | 156(43.5) | 57(43.5) | 99(43.4) |  |
| Histological type, n (%) |  |  |  | 0.258 |
| ADC | 318(88.6) | 118(90.1) | 200(87.7) |  |
| SCC | 13(3.6) | 2(1.5) | 11(4.8) |  |
| SCLC | 14(3.9) | 4(3.1) | 10(4.4) |  |
| Other types | 14(3.9) | 7(5.3) | 7(3.1) |  |
| Treatment line, n (%) |  |  |  | 0.376 |
| First-line | 289(80.5) | 104(79.4) | 185(81.1) |  |
| Second-line | 55(15.3) | 19(14.5) | 36(15.8) |  |
| Third-line and above | 15(4.2) | 8(6.1) | 7(3.1) |  |
| BP treatment duration, n (%) |  |  |  | **<0.001** |
| BP ≤ 24m | 187(52.1) | 97(74.0) | 90(39.5) |  |
| BP > 24m | 172(47.9) | 34(26.0) | 138(60.5) |  |
| Type of BP, n (%) |  |  |  | **0.007** |
| ZOL | 179(49.9) | 53(40.5) | 126(55.3) |  |
| Others | 180(50.1) | 78(59.5) | 102(44.7) |  |

Note: Differences between variables were calculated using the Wilcoxon test or chi-square test. IQR, interquartile range; ADC, adenocarcinoma; SCC, squamous cell carcinoma; SCLC, small cell lung cancer; BP, bisphosphonate; ZOL, zoledronic acid.

**Figure legends**

**Supplementary Figure S1 AE-free survivals of patients with two BP treatment patterns in different subtypes.** The comparison was performed by the log-rank test. OS, overall survival; BP, bisphosphonate; AE, adverse event.

**Supplementary Figure S2 The Kaplan-Meier curves for SRE-free survivals of patients with regular and irregular therapy modes stratified by different OS and infusion times.** Statistical analysis was performed using the log-rank test. OS, overall survival; BP, bisphosphonate; SRE, skeletal-related event.



**Supplementary Figure S1**



**Supplementary Figure S2**