Supplementary Table S1. Name of participating hospitals

| No | Name of participating hospitals |
|---|---|
| 1 | the First Affiliated Hospital with Nanjing Medical University |
| 2 | Guangdong Provincial People's Hospital |
| 3 | The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital |
| 4 | Guangdong Provincial Hospital of Chinese Medicine |
| 5 | Liaoning Cancer Hospital &Institute |
| 6 | Union Hospital Tongji Medical College Huazhong University of Science and Technology |
| 7 | Tianjin Medical University Cancer Institute and Hospital |
| 8 | The First Affiliated Hospital of the University of Science and Technology of China |

Supplementary Table S2. Patient Baseline Demographic and Disease Characteristics

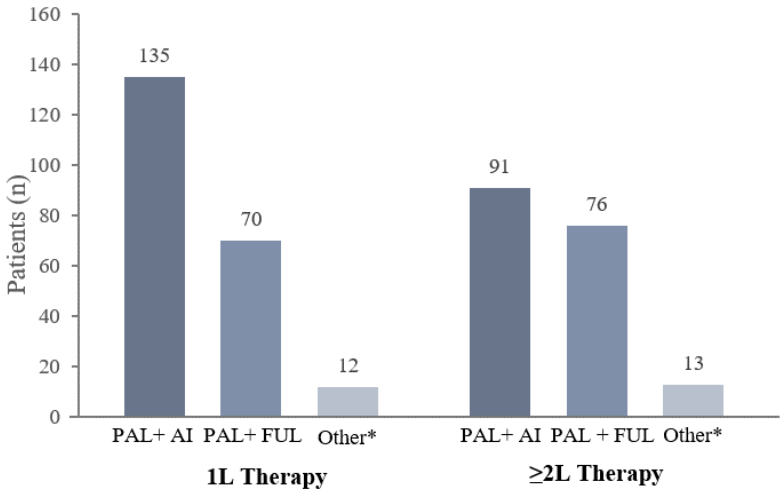
| Characteristic | Patients (N=397) | |
|---|---|---|
| BMI *, n (%) | | |
| Underweight | | 25(6.30) |
| Normal weight | | 211(53.15) |
| Overweight | | 115(28.97) |
| Obesity | 26 | (6.55) |
| Not reported | 20 | (5.04) |
| Methods of castration | | |
| Natural | 230 | (57.93) |
| Chemical | 131 | (33.00) |
| Surgical | 36 | (9.07) |
| Underlying disease | | |
| Yes | 88 | (22.17) |
| No | 309 | (77.83) |
| Operation mode | | |
| Conserving surgery | 27 | (6.80) |
| Modified radical mastectomy | 203 | (51.13) |
| Radical mastecomy | 22 | (5.54) |
| Total mastectomy | 19 | (4.79) |
| Else | 20 | (5.04) |
| Unknown | 16 | (4.03) |
| Expression of estrogen receptor (ER) | | |
| Negative (<1%) | 3 | (0.76) |
| Low-Positive (1%-10%) | 8 | (2.02) |
| High-Positive (>10%) | 378 | (95.21) |
| Unknown | 8 | (2.02) |
| HER2 status | | |
| Positive | 26 | (6.55) |

| | | |
|---|---|---|
| Weak positive | 202 | (50.88) |
| Negative | 161 | (40.55) |
| Unknown | 8 | (2.02) |
| Ki67 index | | |
| Low (<15%) | 73 | (18.39) |
| Mediation (15%-30%) | 132 | (33.25) |
| high (>30%) | 159 | (40.05) |
| Unknown | 33 | (8.31) |
| Prior neoadjuvant therapy, n (%) | | |
| Yes | 50 | (12.59) |
| No | 250 | (62.97) |
| Not reported | 7 | (1.76) |
| Prior adjuvant radiotherapy, n (%) | | |
| Yes | 158 | (39.80) |
| No | 143 | (36.02) |
| Not reported | 6 | (1.51) |
| Adjuvant endocrine regimen | | |
| Tamoxifen | 112 | (28.21) |
| Letrozole | 63 | (15.87) |
| Anastrozole | 27 | (6.80) |
| Exemestane | 29 | (7.30) |
| Toremifene | 24 | (6.05) |
| Tamoxifen followed by aromatase inhibitors | 8 | (2.02) |
| Duration of adjuvant endocrine therapy | 249 | |
| Less than 60 months | 171 | (43.07) |
| Equal to 60 months | 50 | (12.59) |
| More than 60 months | 28 | (7.05) |
| Reasons for discontinuation of adjuvant endocrine therapy | | |
| Treatment completed | 56 | (14.11) |
| Disease progression | 140 | (35.26) |
| Intolerable adverse events | 2 | (0.50) |
| Patients' willing | 21 | (5.29) |
| Else | 24 | (6.05) |
| Unknown | 10 | (2.52) |
| Line of chemotherapy before CDK4/6i treatment | | |
| Untreated | 188 | (47.36) |
| 1L | 107 | (26.95) |
| ≥2L | 99 | (24.94) |
| Unknown | 3 | (0.76) |
| Re-operate before CDK4/6i treatment | | |
| Yes | 52 | (13.10) |
| No | 310 | (78.09) |
| Unknown | 35 | (8.82) |

| | | |
|---|---|---|
| Re-radiotherapy before CDK4/6i treatment | | |
| Yes | 47 | (11.84) |
| No | 314 | (79.09) |
| Unknown | 36 | (9.07) |
| AI use history | | |
| Yes | 205 | (51.64) |
| No | 192 | (48.36) |

* Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters (kg/m2). Underweight is a BMI less than 18.5, normal Weight is a BMI from 18.5 to 24.9, overweight is a BMI greater than or equal to 25, and obesity is a BMI greater than or equal to 30.

Supplementary Figure S1. Treatment patterns in Chinese real-world population




AI, aromatase inhibitors (including letrozole, anastrozole, or exemestane); FUL, fulvestrant.

* Represents patients who, at the onset of the study, received PAL with hormone combinations other than letrozole, anastrozole, exemestane, or fulvestrant or received PAL without hormone combinations.

Supplementary Table S3. Treatment characteristics of Palbociclib

| Characteristic | Patients (N=397) | |
|---|---|---|
| Combination therapy | | |
| Fulvestrant | 148 | (37.28) |
| Letrozole | 103 | (25.94) |
| Anastrozole | 52 | (13.10) |
| Exemestane | 71 | (17.88) |
| Along | 17 | (4.28) |
| Else | 6 | (1.51) |
| Treatment discontinuation | | |
| Yes | 230 | (57.93) |
| Reason for discontinuation | | |
| Disease progression | 172 | (43.32) |

| | | |
|---|---|---|
| Intolerable adverse events | 12 | (3.02) |
| Economy | 19 | (4.79) |
| Patients' willing | 8 | (2.02) |
| Lost to follow-up | 3 | (0.76) |
| Physician's choice | 13 | (3.27) |
| Unknown | 3 | (0.76) |

Supplementary Table S4. Univariate analysis for independent factors of PAL

| | All (n = 397) | | Primary resistance (n = 72) | | | Secondary resistance (n= 231) | | |
|---|---|---|---|---|---|---|---|---|
| | mPFS (mo) | P values | n (%) | mPFS (mo) | P values | n (%) | mPFS (mo) | P values |
| BMI | | 0.7432 | | | 0.6149 | | | 0.8147 |
| <24 | 13.63 | | 43 (59.72%) | 9.13 | | 141 (61.04%) | 13.43 | |
| ≥24 | 14.17 | | 29 (40.28%) | 9.13 | | 90 (38.96%) | 14.77 | |
| Underlying disease | | 0.2832 | | | 0.2121 | | | 0.4292 |
| Yes | 18.77 | | 15 (20.83%) | 15.23 | | 53 (22.94%) | 17.23 | |
| No | 13.50 | | 57 (79.17%) | 8.1 | | 178 (77.06%) | 13.27 | |
| Menopausal status at study entry | | 0.2191 | | | 0.4217 | | | 0.3865 |
| Premenopasual | 16.03 | | 20 (27.78%) | 8.73 | | 46 (19.91%) | 14.5 | |
| Perimenopausal | 10.63 | | 7 (9.72%) | 5.63 | | 33 (14.29%) | 10.33 | |
| Postmenopausal | 14.20 | | 45 (62.50%) | 9.13 | | 152 (65.80%) | 14.23 | |
| Methods of castration | | 0.3784 | | | 0.4225 | | | 0.6170 |
| Natural | 14.04 | | 36 (50.00%) | 9.5 | | 135 (58.44%) | 13.5 | |
| Artificial | 14.23 | | 36 (50.00%) | 5.63 | | 96 (41.56%) | 14.23 | |
| ECOG | | 0.1123 | | | 0.0689 | | | 0.8584 |
| ≤1 | 14.5 | | 60 (83.33%) | 9.33 | | 186 (80.52%) | 13.43 | |
| ≥2 | 10.77 | | 12 (16.67%) | 6.13 | | 45 (19.48%) | 14.77 | |
| Pathology | | 0.9198 | | | 0.5858 | | | 0.9546 |
| Invasive ductal carcinoma (IDC) | 14.23 | | 33 (45.83%) | 9.33 | | 107 (46.32%) | 14.2 | |
| Invasive lobular carcinoma (ILC) | 14.47 | | 13 (18.06%) | 10.3 | | 31 (13.42%) | 14.23 | |
| Else | 13.43 | | | | | | | |
| Hormone receptor status changes in Secondary pathological | | 0.6144 | | | | | | |
| Down-regulation | 11.73 | | | | | | | |
| Consistency | 13.43 | | | | | | | |
| Up-regulation | 12.73 | | | | | | | |
| HER2 status | | 0.7355 | | | | | | |
| Positive | 13.20 | | | | 0.3797 | | | 0.9282 |
| Weak positive | 13.27 | | 40 (55.56%) | 8.17 | | 108 (46.75%) | 13.27 | |
| Negative | 14.23 | | 28 (38.89%) | 9.33 | | 102 (44.16%) | 13.5 | |
| T | | 0.2121 | | | 0.4272 | | | |
| T1 | 11.70 | | 17 (23.61%) | 10.3 | | | | |
| T2 | 13.13 | | 30 (41.67%) | 8.73 | | | | |

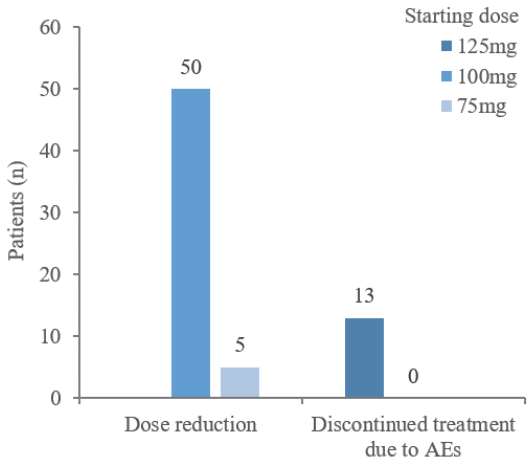
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| T3 | Not reached | | 3 | (4.17%) | 4.37 | | | | | |
| T4 | 14.23 | | | | | | | | | |
| N | | 0.3064 | | (0.00%) | | 0.1902 | | | | |
| N0 | 14.33 | | 11 | | 13.7 | | | | | |
| N1 | 13.13 | | 16 | (22.22%) | 5.47 | | | | | |
| N2 | 11.73 | | 12 | (16.67%) | 5.57 | | | | | |
| N3 | 10.73 | | 16 | (22.22%) | 8.17 | | | | | |
| Prior neoadjuvant therapy | | 0.2603 | | | | 0.3261 | | | | 0.7874 |
| Yes | 13.27 | | 16 | (22.22%) | 4.97 | | 31 | (13.42%) | 14.23 | |
| No | 14.33 | | 54 | (75.00%) | 10.3 | | 191 | (82.68%) | 13.43 | |
| Prior adjuvant chemotherapy, n (%) | | 0.1492 | | | | 0.8690 | | | | 0.1879 |
| Yes | 13.70 | | 53 | (73.61%) | 8.73 | | 178 | (77.06%) | 14.5 | |
| No | 18.30 | | 18 | (25.00%) | 11.2 | | 47 | (20.35%) | 12.1 | |
| Prior adjuvant ET, n (%) | | 0.4516 | | | | | | | | 0.1202 |
| Yes | 13.40 | | | | | | 178 | (77.06%) | 16.03 | |
| No | 14.50 | | | | | | 20 | (8.66%) | 10.77 | |
| Duration of endocrine therapy | | | | | | | | | | 0.2715 |
| < 5 years | | | | | | | 106 | (45.89%) | 14.23 | |
| 5 years | | | | | | | 53 | (22.94%) | 20.37 | |
| > 5 years | | | | | | | 38 | (16.45%) | 12.83 | |
| Adjuvant endocrine regimen | | 0.8776 | | | | | | | | |
| Tamoxifen | 14.07 | | 18 | (25.00%) | 9.13 | | 93 | (40.26%) | 16.67 | |
| Letrozole | 12.83 | | 23 | (31.94%) | 9.33 | | 41 | (17.75%) | 12.83 | |
| Anastrozole | 21.37 | | 11 | (15.28%) | 7.03 | | 17 | (7.36%) | Not achieved | |
| Exemestane | 16.03 | | 7 | (9.72%) | 4.8 | | 22 | (9.52%) | 18.33 | |
| Toremifene | 14.20 | | 9 | (12.50%) | 6.13 | | 19 | (8.23%) | 18.33 | |
| TAM-AI | 11.70 | | | | | | 7 | (3.03%) | 11.7 | |
| Site of metastases | | | | | | | | | | |
| Lung metastases | | 0.4565 | | | | 0.3465 | | | | 0.7573 |
| Yes | 16.67 | | 16 | (22.22%) | 13.7 | | 89 | (38.53%) | 13.43 | |
| No | 13.40 | | 56 | (77.78%) | 8.1 | | 142 | (61.47%) | 14.2 | |
| Brain metastases | | 0.5245 | | | | | | | | 0.4576 |
| Yes | 12.73 | | | | | | 21 | (9.09%) | 12.02 | |
| No | 14.23 | | | | | | 210 | (90.91%) | 14.2 | |
| Lymph node metastasis | | 0.5185 | | | | 0.8583 | | | | 0.2035 |
| Yes | 13.50 | | 14 | (19.44%) | 8.17 | | 83 | (35.93%) | 13.5 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| No | 14.23 | | 58 | (80.56%) | 9.13 | | 148 | (64.07%) | 13.43 | |
| Re-operate before CDK4/6i treatment | | 0.6250 | | | | 0.1010 | | | | 0.1996 |
| Yes | 14.77 | | 6 | (8.33%) | 4.8 | | 39 | (16.88%) | 16.67 | |
| No | 14.20 | | 66 | (91.67%) | 9.13 | | 178 | (77.06%) | 13.27 | |
| Dose reduction | | 0.0640 | | | | 0.2358 | | | | 0.4232 |
| Yes | 21.37 | | 59 | (81.94%) | 13.7 | | 30 | (12.99%) | 16.67 | |
| No | 13.43 | | 13 | (18.06%) | 8.17 | | 201 | (87.01%) | 13.4 | |
| Adverse events Grade 3/4 | | 0.3260 | | | | 0.3197 | | | | 0.5703 |
| Yes | 13.70 | | 32 | (44.44%) | 9.13 | | 118 | (51.08%) | 14.23 | |
| No | 14.23 | | 40 | (55.56%) | 8.17 | | 113 | (48.92%) | 13.13 | |

Supplementary Table S5. The Wilcoxon signed-rank test for the distribution of adverse events in the elderly population and the general population

| | Age | N | Median (P25, P75) | Z | P value |
|---|---|---|---|---|---|
| Neutrophil count decreased | <65 | 235 | 2 (1, 3) | 1.116 | 0.265 |
| | ≥65 | 72 | 2 (1, 3) | | |
| White blood cell decreased | <65 | 229 | 2 (0, 2.5) | 1.113 | 0.266 |
| | ≥65 | 66 | 2 (1, 3) | | |
| Anemia | <65 | 95 | 0 (0, 1) | -1.649 | 0.099 |
| | ≥65 | 37 | 0 (0, 1) | | |
| Platelet count decreased | <65 | 89 | 0 (0, 1) | -0.31 | 0.757 |
| | ≥65 | 28 | 0 (0, 1) | | |

Supplementary Figure S2. Palbociclib dose adjustment




Supplementary Table S6. The X2 test for the relationship between the initial diagnosis stage and line of Palbociclib

| | 1L (N = 217) | ≥2L (N = 180) | P value |
|---|---|---|---|
| Recurrent from earlier stages | 154 | 153 | 0.001 |
| De novo | 63 | 27 | |