**Supplementary Table 1.** Summary of phase III clinical trials of targeted therapies in hormone-receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Line | Trial | Description | *n* | Menopausal status | Median PFS;  Hazard ratio (95% CI) | OS;  Hazard ratio (95% CI) | ORR (%) |
| 1st | PALOMA-2  MONALEESA-2  MONALEESA-7  MONARCH-3  HORIZON | Palbociclib + letrozole  *vs.* placebo + letrozole  Ribociclib + letrozole  *vs.* placebo + letrozole  Ribociclib + OFS + tamoxifen/AI *vs.* placebo + OFS + tamoxifen/AI  Abemaciclib + NASI  *vs.* placebo + NASI  Temsirolimus + letrozole  *vs.* placebo + letrozole | 666  668  672  493  1112 | PMP  PMP  Pre-MP  PMP  PMP | 24.8 *vs.* 14.5 months;  0.58 (0.46−0.72)  25.3 vs. 16.0 months;  0.57 (0.46−0.70)  23.8 vs. 13.0 months;  0.55 (0.44−0.69)  28.2 *vs.* 14.8 months;  0.54 (0.42−0.70)  8.9 *vs.* 9.0 months;  0.9 (0.76−1.07) | NR  NR  NR *vs.* 40.9 months;  0.71 (0.54−0.95)  NR  NR | 55.0 *vs.* 39.0  54.5 *vs.* 38.8  41.0 *vs.* 30.0  61.0 *vs.* 45.5  27 *vs.* 27 |
| 2nd | PALOMA-3  MONALEESA-3  MONARCH-2  BOLERO-2  BELLE-2  BELLE-3  SANDPIPER  SOLAR-1  ACE | Palbociclib + fulvestrant ± OFS  *vs.* placebo + fulvestrant ± OFS  Ribociclib + fulvestrant  *vs.* placebo + fulvestrant  Abemaciclib + fulvestrant ± OFS  *vs.* placebo + fulvestrant ± OFS  Everolimus + exemestrane  *vs.* placebo + exemestrane  Buparlisib + fulvestrant  *vs.* placebo + fulvestrant  Buparlisib + fulvestrant  *vs.* placebo + fulvestrant  Taselisib + fulvestrant  *vs.* placebo + fulvestrant  Alpelisib + fulvestrant  *vs.* placebo + fulvestrant  Chidamide + exemestane  *vs.* placebo + exemestane | 521  726  669  724  1147  432  516\*  341\*  365 | PMP + Pre-MP  PMP  PMP + Pre-MP  PMP  PMP  PMP  PMP  PMP  PMP | 9.5 *vs*. 4.6 months;  0.46 (0.36−0.59)  20.5 *vs*. 12.8 months;  0.59 (0.48−0.73)  16.4 *vs*. 9.3 months;  0.55 (0.45−0.68)  7.8 *vs*. 3.2 months;  0.45 (0.38−0.54)  6.9 *vs.* 5.0 months;  0.78 (0.67−0.89)  3.9 *vs.* 1.8 months;  0.67 (0.54−0.84)  7.4 *vs.* 5.4 months;  0.70 (0.56−0.89)  11.0 *vs.* 5.7 months;  0.65 (0.50−0.85)  7.4 *vs.* 3.8 months;  0.75 (0.58−0.98) | 34.9 *vs.* 28.0 months;  0.81 (0.64−1.03)  NR  NR  31.0 *vs.* 26.6 months;  0.89 (0.73−1.10)  33.2 *vs.* 30.4 months;  0.87 (0.74−1.02)  NR  NR  NR  NR | 24.6 *vs.* 10.9  40.9 *vs.* 28.7  48.1 *vs.* 21.3  12.6 *vs.* 1.7  11.8 *vs.* 7.7  8.0 *vs.* 2.0  28.0 *vs.* 11.9  35.7 *vs.* 16.2  18.4 *vs.* 9.1 |

\*Patients with PIK3CA mutated tumor. PFS: progression free survival; CI: confidence interval; OS: overall survival; ORR: objective response rate; PMP: post-menopausal; Pre-MP: pre-menopausal; NR: not reported; OFS: ovarian function suppression; NASI: nonsteroidal aromatase inhibitor.