

## **Supplementary information**

**Supplemental Table S1.** Subgroup analysis of progression-free survival for three CDK4/6 inhibitors.

**Supplemental Figure S1.** Forest plot comparison of three CDK4/6 inhibitors.

**Supplemental Figure S2.** Sensitivity analysis.

**Supplemental Table S1** Subgroup analysis of progression-free survival for three CDK4/6 inhibitors

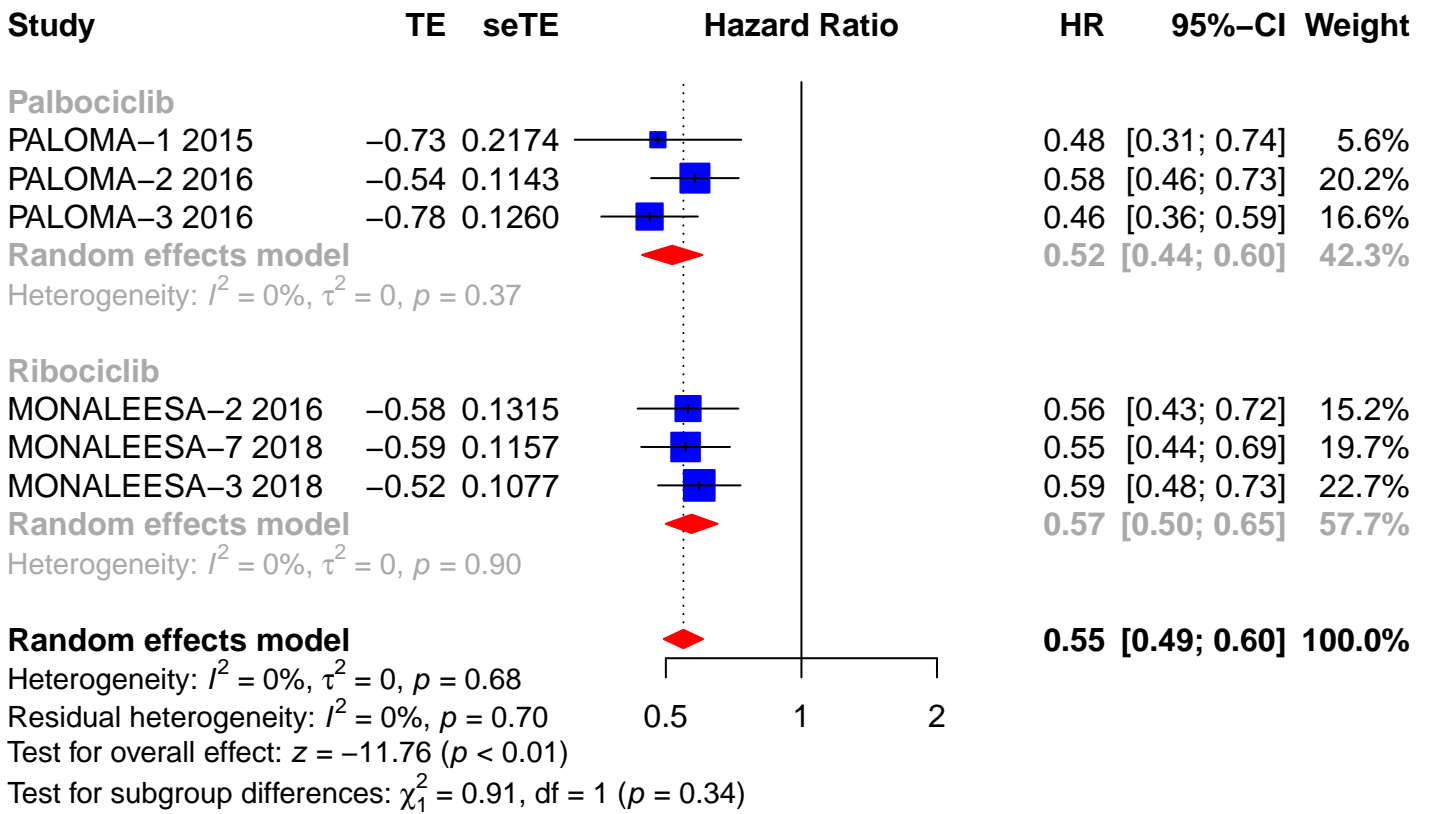
Subgroup	Pooled Hazard Ratio for PFS (95% CI)		
	Palbo+ET vs ET	Ribo+ET vs ET	Abema+ET vs ET
Age			
<65 yr	0.44(0.25-0.79)	0.57(0.46-0.70)	0.53(0.42-0.65)
≥65 yr	0.55(0.40-0.77)	0.60(0.47-0.78)	0.60(0.46-0.79)
Race			
White	0.58(0.45-0.74)	0.60(0.52-0.70)	0.64(0.52-0.80)
Asian	0.48(0.27-0.86)	0.57(0.27-1.18)	0.41(0.24-0.69)
Other	-	0.88(0.20-3.9)	0.30(0.12-0.8)
Region			
North America	0.60(0.43-0.84)	0.54(0.29-1.01)	0.49(0.33-0.73)
Europe	0.57(0.41-0.80)	0.63(0.44-0.91)	0.62(0.45-0.85)
Asia	0.49(0.27-0.88)	0.42(0.27-0.66)	0.52(0.36-0.75)
ECOG performance status			
0	0.57(0.39-0.83)	0.56(0.48-0.66)	0.51(0.41-0.63)
1	0.50(0.38-0.66)	0.56(0.45-0.71)	0.62(0.48-0.80)
Site of metastatic disease			
Visceral	0.55(0.45-0.67)	0.57(0.48-0.68)	0.52(0.42-0.65)
Bone only	0.35(0.22-0.55)	0.55(0.37-0.84)	0.55(0.38-0.80)
Nonvisceral	0.46(0.36-0.59)	0.58(0.48-0.71)	-
Other	0.40(0.20-0.81)	0.58(0.50-0.67)	0.54(0.22-1.30)
Prior chemotherapy	Prior chemotherapy		
Yes	0.54(0.44-0.68)	0.55(0.41-0.74)	-
No	0.44(0.29-0.67)	0.56(0.46-0.70)	
Prior endocrine therapy			
Yes	0.52(0.40-0.68)	0.59(0.47-0.73)	-
No	0.52(0.33-0.81)	0.55(0.45-0.67)	0.51(0.34-0.76)
Prior aromatase inhibitor	0.45(0.32-0.62)	0.61(0.50-0.73)	0.42(0.24-0.73)
Prior tamoxifen	0.57(0.41-0.79)	0.60(0.48-0.74)	0.92(0.50-1.70)
No. of disease sites			
1	0.53(0.38-0.72)	-	0.54(0.38-0.76)
2	0.37(0.24-0.58)	0.59(0.45-0.77)	0.41(0.29-0.60)
≥3	0.50(0.33-0.76)	0.62(0.44-0.87)	0.75(0.52-1.08)
Disease-free interval (≤12 mo)	0.46(0.34-0.63)	0.56(0.37-0.86)	-
Disease-free interval	0.50(0.36-0.68)	0.62(0.46-0.83)	-

(>12 mo)			
Disease setting (De Novo Metastatic)	-	0.45(0.27-0.75)	0.49(0.31-0.77)
Disease setting (Metastatic Recurrent)	-	0.60(0.45-0.80)	0.59(0.41-0.85)
Pre-or perimenopause	0.50(0.29-0.87)	-	0.42(0.25-0.70)
Postmenopausal	0.45(0.34-0.59)	-	0.58(0.46-0.73)
PgR status (Positive)	-	0.59(0.49-0.71)	0.59(0.49-0.72)
PgR status (Negative)	-	0.40(0.27-0.60)	0.48(0.34-0.68)
Measurable disease (Yes)	0.66(0.52-0.84)	-	0.53(0.44-0.64)
Measurable disease (No)	0.35(0.22-0.56)	-	0.59(0.41-0.84)
Previous systemic therapy (Yes)	0.45(0.35-0.57)	-	-
Previous systemic therapy (No)	0.44(0.27-0.70)	-	-

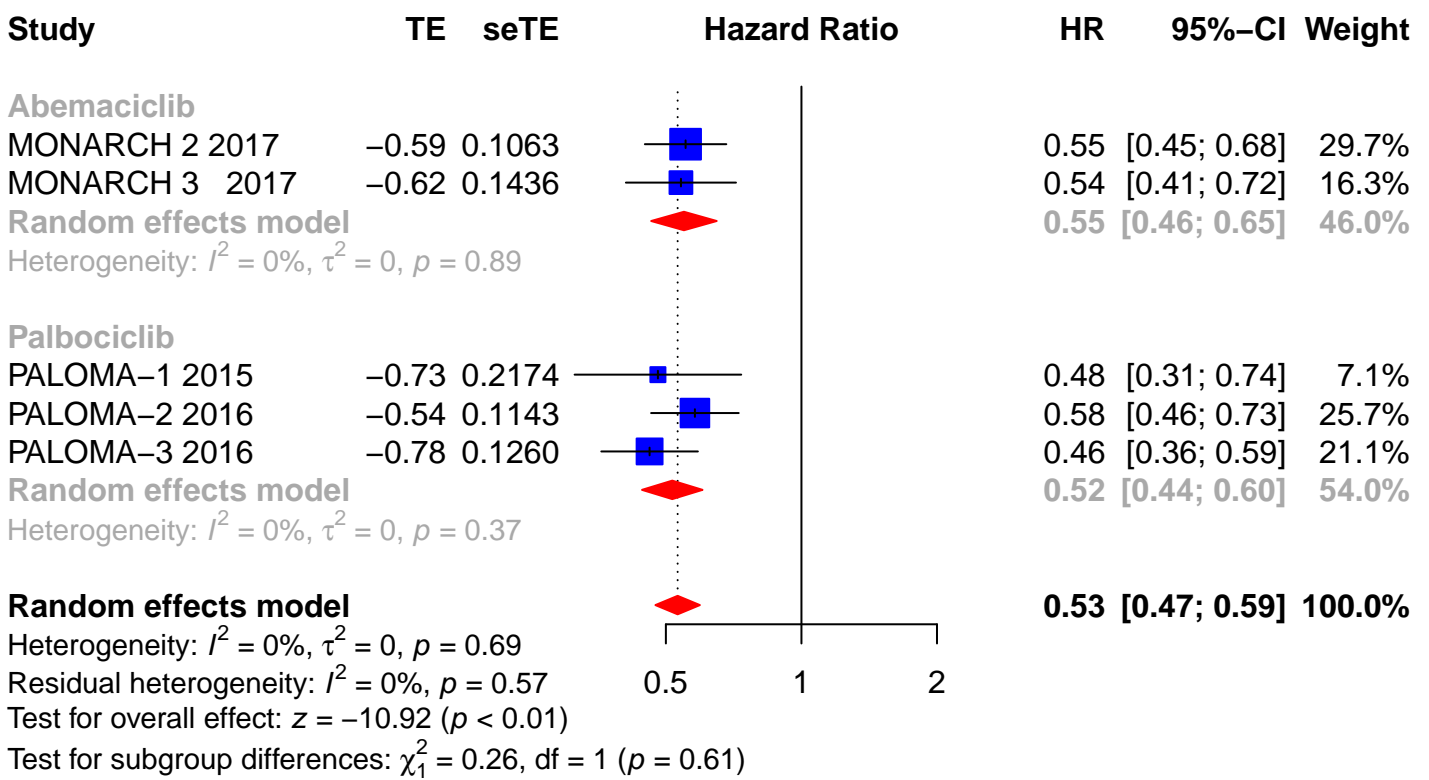
**Abbreviations:** PFS, progression-free survival; CI, confidence interval; yr, year; Palbo, palbociclib; Ribo, ribociclib; Abema, abemaciclib; AI, aromatase inhibitors; Ful, fulvestrant; ET, endocrine therapy; ECOG, Eastern Cooperative Oncology Group; mo, months; PgR, progesterone receptor.

Supplemental Figure S1. Forest plot comparison of three CDK46 inhibitors.

A



B



C

