

Supplementary information

Supplementary Material S1: search strategies

Database	Search Strategy
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Scopus

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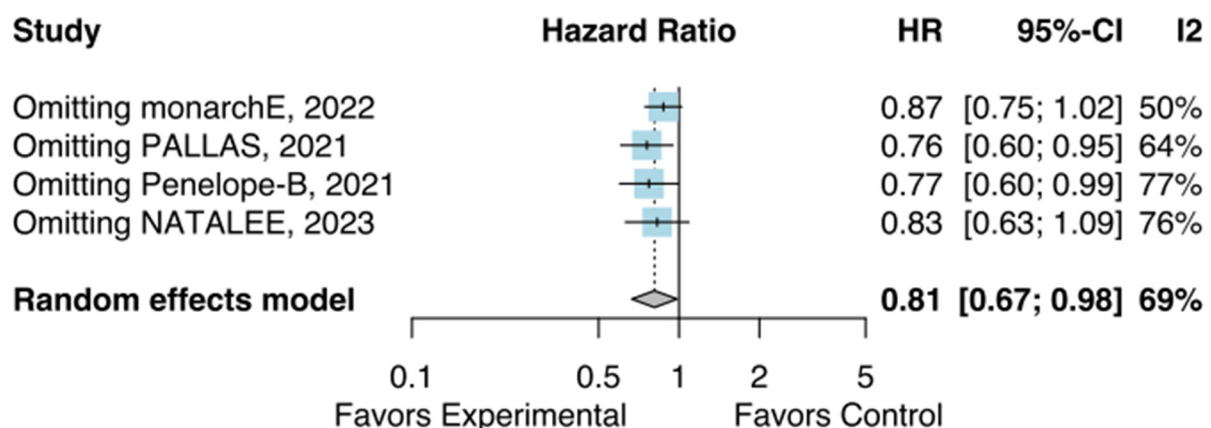
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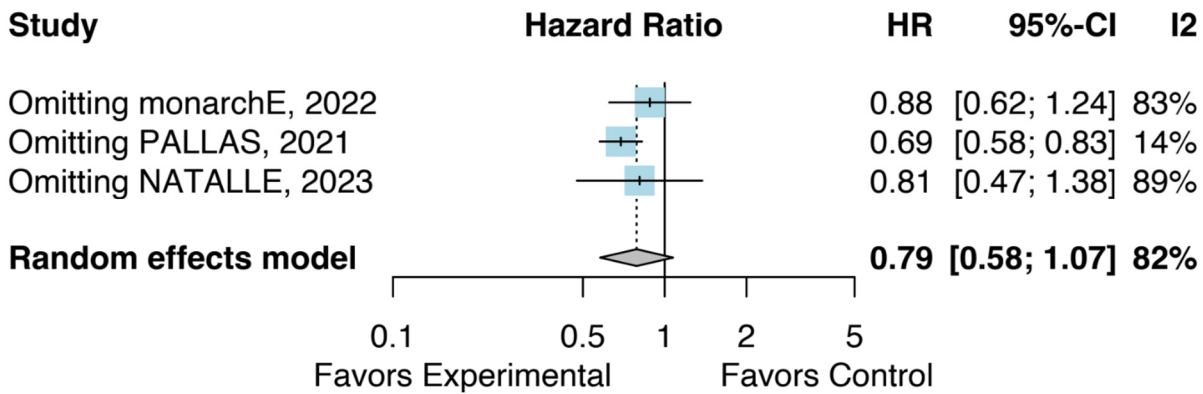
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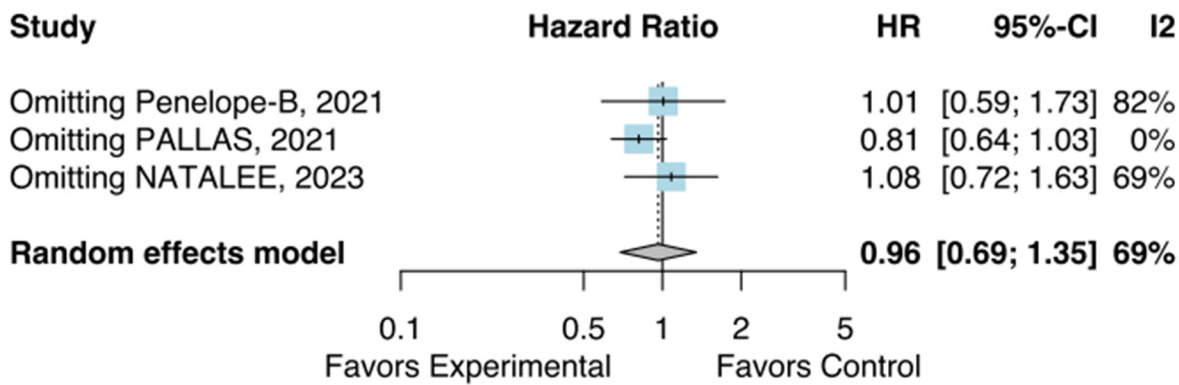
Supplementary Material S2: leave-one-out sensitive-analysis of invasive disease-free survival



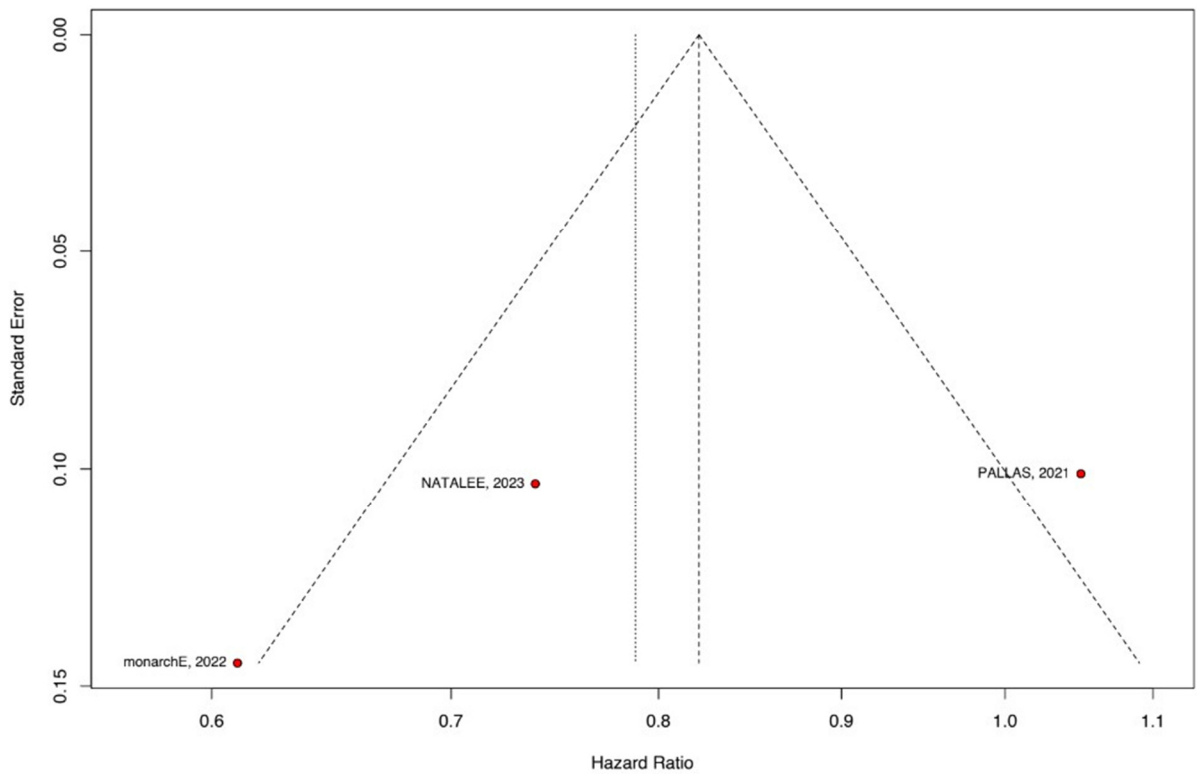
Supplementary Material S3: leave-one-out sensitive-analysis of distant relapse-free survival



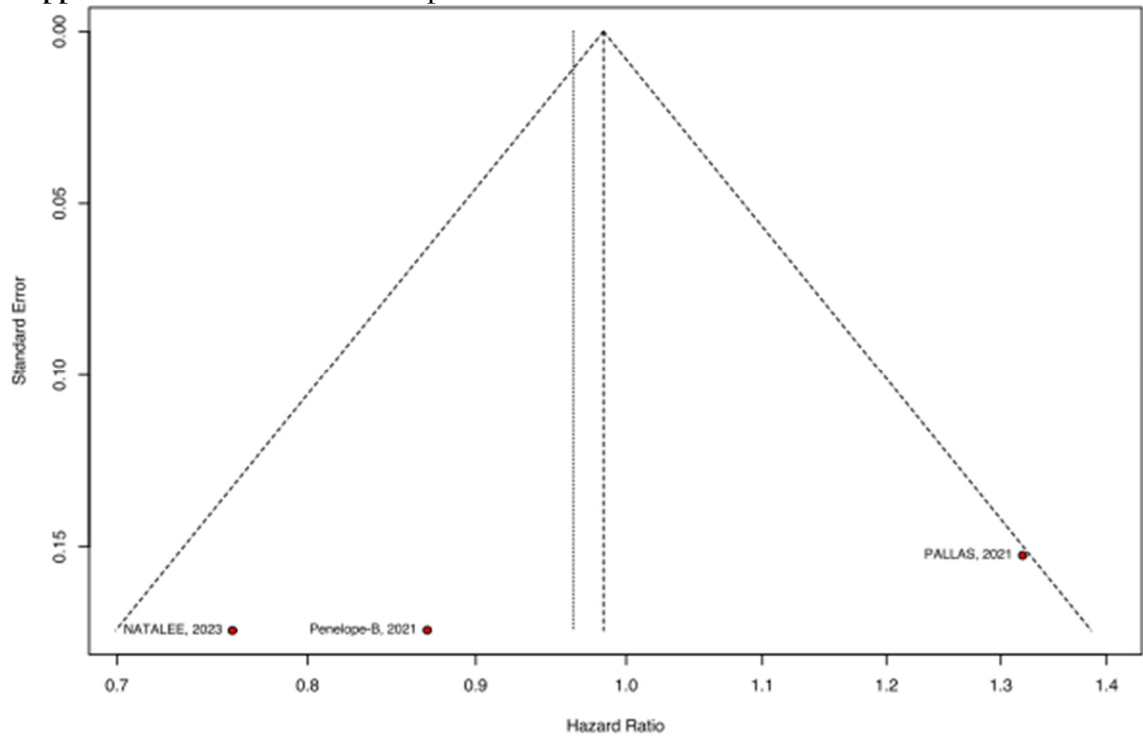
Supplementary Material S4: leave-one-out Sensitive-Analysis of Overall Survival:



Supplement Material S5: funnel plot of distant relapse-free survival



Supplement Material S6: funnel plot of overall survival



Supplementary Material S7: GRADE analysis

CDK 4/6 inhibitors + ET compared to ET alone for early ER+, HER- breast cancer

Patient or population: early ER+, HER- breast cancer

Setting: hospital

Intervention: CDK 4/6 inhibitors + ET

Comparison: ET alone

Outcomes	Number of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with ET alone	Risk difference with CDK 4/6 inhibitors + ET
Overall Survival (OS) assessed with: Hazard ratio	12112 (3 RCTs)	⊕⊕⊕○ Moderate ^a	HR 0.96 (0.69 to 1.35) [OS]	Low	
				80 per 100	1 more per 100 (6 fewer to 6 more)
Invasive disease-free survival (iDFS) assessed with: Hazard ratio	14168 (4 RCTs)	⊕⊕⊕○ Moderate ^b	HR 0.81 (0.67 to 0.98) [iDFS]	Low	
				60 per 100	6 more per 100 (1 more to 11 more)
Distant relapse-free survival (DRFS) assessed with: Hazard ratio	12918 (3 RCTs)	⊕⊕⊕○ Moderate ^c	HR 0.79 (0.58 to 1.07) [DRFS]	Low	
				52 per 100	8 more per 100 (2 fewer to 16 more)

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **HR:** hazard Ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.