

EFFICACY AND SAFETY OF CARBOPLATIN-CONTAINING CHEMOTHERAPY IN TRIPLE-NEGATIVE BREAST CANCER: A COMPREHENSIVE SYSTEMATIC REVIEW, META-ANALYSIS, AND TRIAL SEQUENTIAL ANALYSIS WITH BRCA/HRD SUBGROUP ASSESSMENT

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BACKGROUND

TNBC lacks ER, PR, HER2 (~15–20% of cases); higher recurrence, poorer survival.

Carboplatin may exploit HRD in TNBC; effects on survival/toxicity remain unclear.

Objective: evaluate carboplatin's efficacy/safety in TNBC, with TSA and BRCA/HRD subgroup analysis.

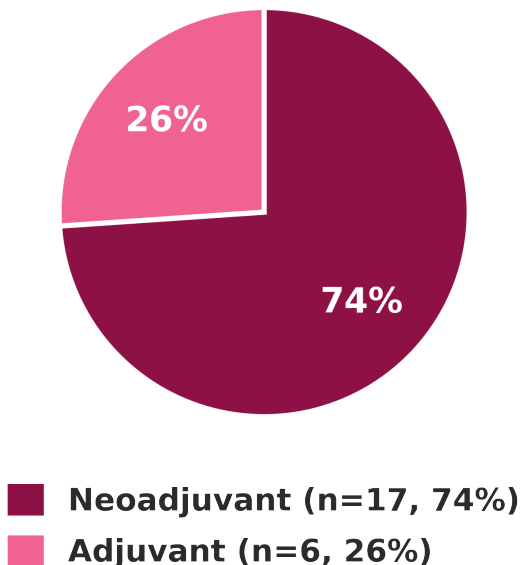
METHODS

- PRISMA review; PROSPERO CRD420261335251
 - 5 databases searched to Feb 2026
 - Phase II/III RCTs vs standard chemo
 - Outcomes: DFS, OS, pCR (random-effects)
 - RoB 2: 6 low, 16 some concerns, 1 high
 - GRADE: high (OS, d-DFS, fatigue, neuropathy); rest moderate/low
- 8,083** records identified
23 studies included
n = 8,797 patients, 23 Phase II/III RCTs.

SECONDARY OUTCOMES

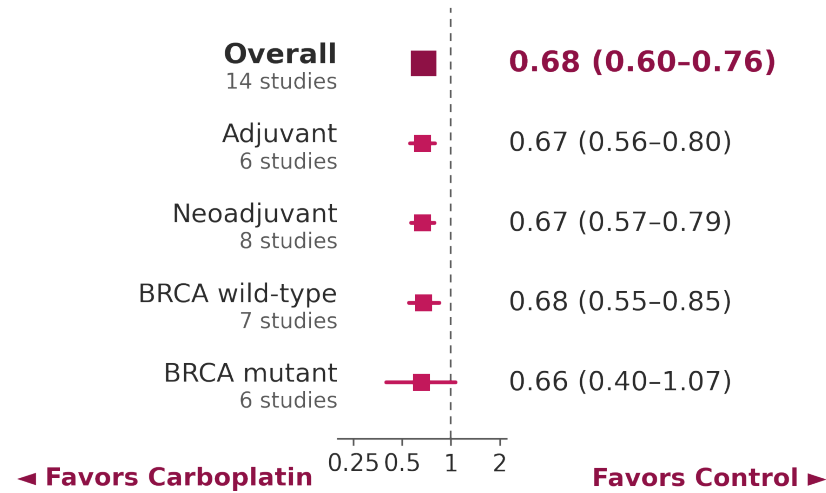
- d-DFS: HR 0.78 (0.63–0.98) — significant
- RFS: HR 0.54 (0.40–0.74) — significant
- i-DFS & ORR: no significant difference
- Dose reduction ↑ (RR 1.77); discontinuation ↑ (RR 1.39)

STUDY DESIGN

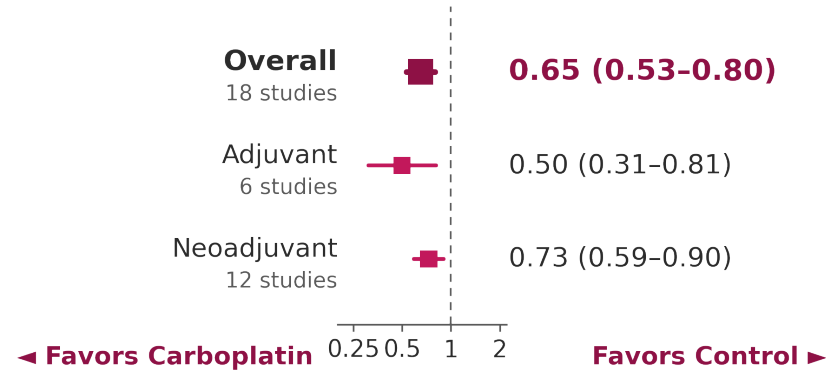


PRIMARY OUTCOMES

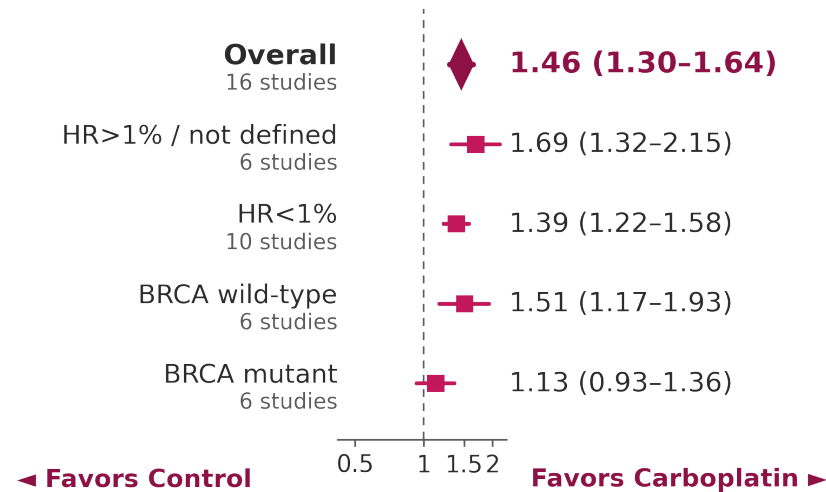
DISEASE-FREE SURVIVAL



OVERALL SURVIVAL



PATHOLOGICAL CR (pCR)



SENSITIVITY ANALYSIS

- DFS: excluding confounded arms (BrighTNess+veliparib, Nasr 2015, CALGB 40603+bevacizumab) -> HR 0.67 (0.59–0.75), I2=3% — robust
- OS: excluding influential study Li 2020 -> HR 0.71 (0.60–0.84), I2=25% — remained significant
- pCR: excluding outlier GeparOcto-GBG 84 -> RR 1.50 (1.35–1.67), I2=25% — slightly stronger effect

TRIAL SEQUENTIAL ANALYSIS

DFS: **CONCLUSIVE**
pCR: **CONCLUSIVE**
OS: **INCONCLUSIVE**

(RIS: DFS 454 events, pCR 3,031 pts, OS 946 events)

BRCA / HRD SUBGROUPS

Group	Figures (95% CI)
BRCA wild-type	DFS: 0.68 (0.55–0.85)* pCR: 1.51 (1.17–1.93)*
BRCA mutant	DFS: 0.66 (0.40–1.07) pCR: 1.13 (0.93–1.36)
HRD positive	DFS: 0.46 (0.22–0.98)*
HRD negative	DFS: 0.62 (0.42–0.91)*

*Significant. Direction consistent across BRCA/HRD strata; magnitude varied — argues against BRCA status alone as sole selection criterion.

SAFETY & TOXICITY

- Anemia RR 4.52 (2.18–9.37)
- Thrombocytopenia RR 4.51 (1.95–10.43)
- Neutropenia RR 1.39 (1.06–1.82)
- Diarrhea RR 1.61 — only non-haematologic AE increased
- No significant ↑ in treatment-related death (RR 1.31) or overall Grade 3/4 AEs
- Fatigue, nausea, vomiting, neuropathy, mucositis: no significant difference

CONCLUSION

Carboplatin gives conclusive, TSA-confirmed benefit for disease-free survival and pathological complete response in TNBC, with a favorable but not yet conclusive overall-survival effect. Hematologic toxicity is increased but generally manageable. BRCA/HRD status may modulate response, arguing against BRCA status alone as the selection criterion — supporting selective, risk-guided use, particularly in node-positive or stage II–III TNBC.