

PLATINUM-BASED NEOADJUVANT CHEMOTHERAPY IN TRIPLE NEGATIVE BREAST CANCER: A SYSTEMATIC REVIEW AND META- ANALYSIS

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Disclosure Information

Relationship Relevant to this Session

Poggio, Francesca:

No relevant relationship to disclose.

Study Background

- The achievement of pathological complete response (pCR) in triple negative breast cancer (TNBC) has a strong prognostic value ^{1,2}.
- Neoadjuvant chemotherapy is considered the preferred approach for TNBC patients, also in the earlier stage ³.
- The role of platinum-based neoadjuvant chemotherapy in TNBC is highly controversial and its use is not endorsed by current guidelines.
- To provide up to date evidence on this controversial topic, we conducted a systematic review and meta-analysis aiming to better elucidate the role of platinum-based neoadjuvant chemotherapy in TNBC patients.

1. Cortazar P, Lancet 2014; 2. von Minckwitz G, J Clin Oncol 2012; 3. Harbeck N, Breast 2017.

Study Design

- Quantitative synthesis of randomized trials evaluating the activity, efficacy and safety of platinum-based (experimental arm) versus platinum free (control arm) neoadjuvant chemotherapy in TNBC patients.
- The work was done and reported according to the PRISMA guidelines for reporting of systematic reviews.
- A literature search using PubMed, Embase and the Cochrane Library was performed with no date restriction up to October 30th, 2017; abstracts presented at ASCO, SABCS and ESMO meetings were also searched.

Eligibility Criteria

- **Inclusion criteria:**
 - a) phase II or III randomized controlled trials (RCTs);
 - b) RCTs including TNBC patients who received platinum-based neoadjuvant chemotherapy in the experimental arm and platinum-free neoadjuvant chemotherapy in the control arm;
 - c) studies with available information on pCR rates in the experimental and control arms to estimate the odds ratio (OR) and 95% confidence intervals (CI).
- **Exclusion criteria:**
 - a) non-randomized controlled trials on this topic;
 - b) RCTs investigating platinum-based neoadjuvant chemotherapy in patients with breast cancer subtypes other than TNBC ;
 - c) ongoing studies with results not presented or published at the time of the literature search.

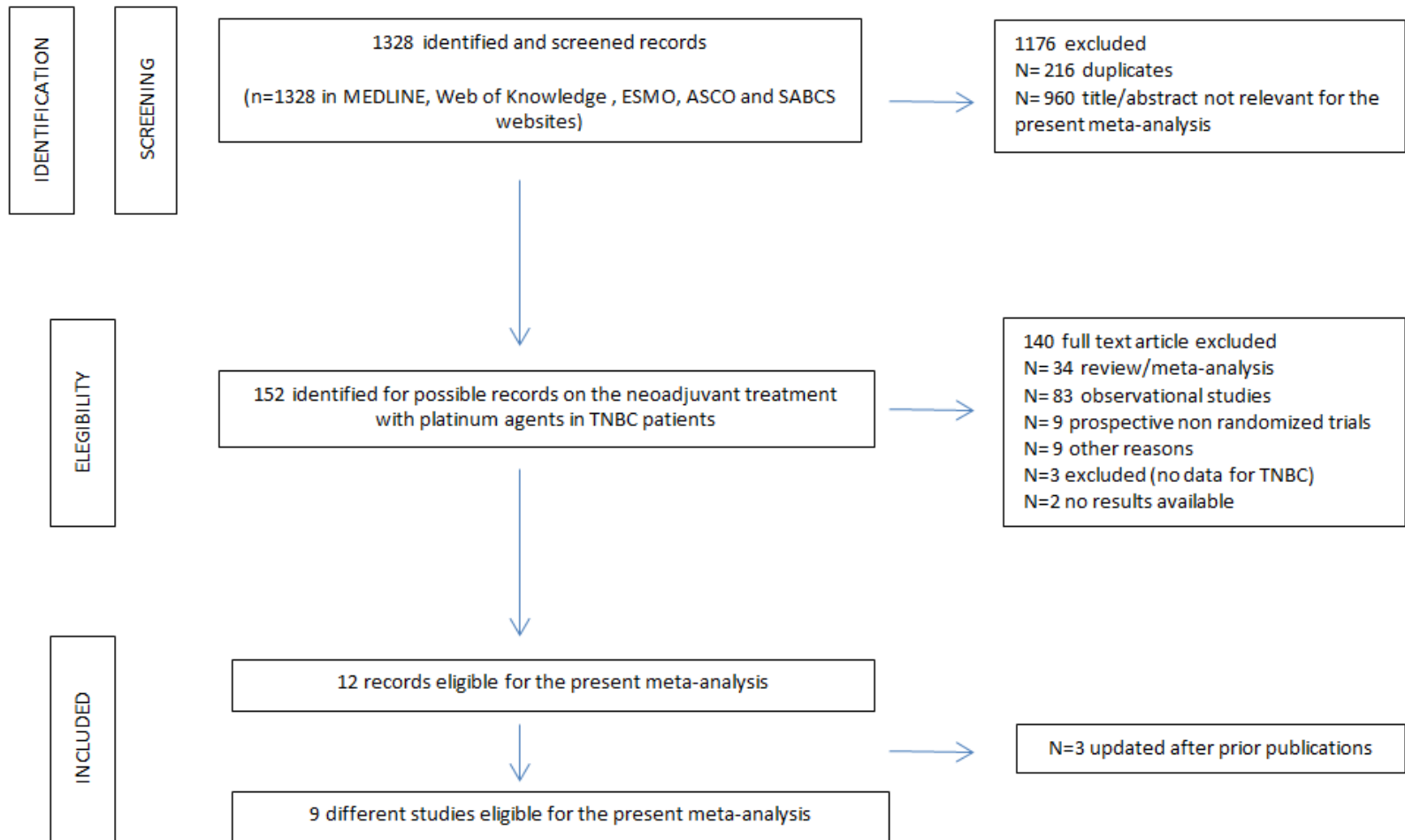
Study Objectives and Endpoints

- **Primary objective:** to compare the activity of platinum-based versus platinum-free neoadjuvant chemotherapy in TNBC patients in term of pCR (i.e. ypT0/is pN0)
- **Secondary objectives:**
 - a) to compare event-free survival (EFS) and overall survival (OS);
 - b) to compare the grade 3 and 4 adverse events (AEs, i.e. neutropenia, anemia, thrombocytopenia and neuropathy)

Statistical Considerations

- ORs and 95% CI were calculated for pCR, ORR, grade 3 and 4 AEs.
- Hazard ratios (HRs) and 95% CI were calculated in terms of EFS and OS.
- In presence of significant heterogeneity among the trials, the method of Der Simonian and Laird using random effect model was performed.
- A visual inspection of the funnel plot and the Harbord's asymmetry test were used to assess the likelihood of publication bias.

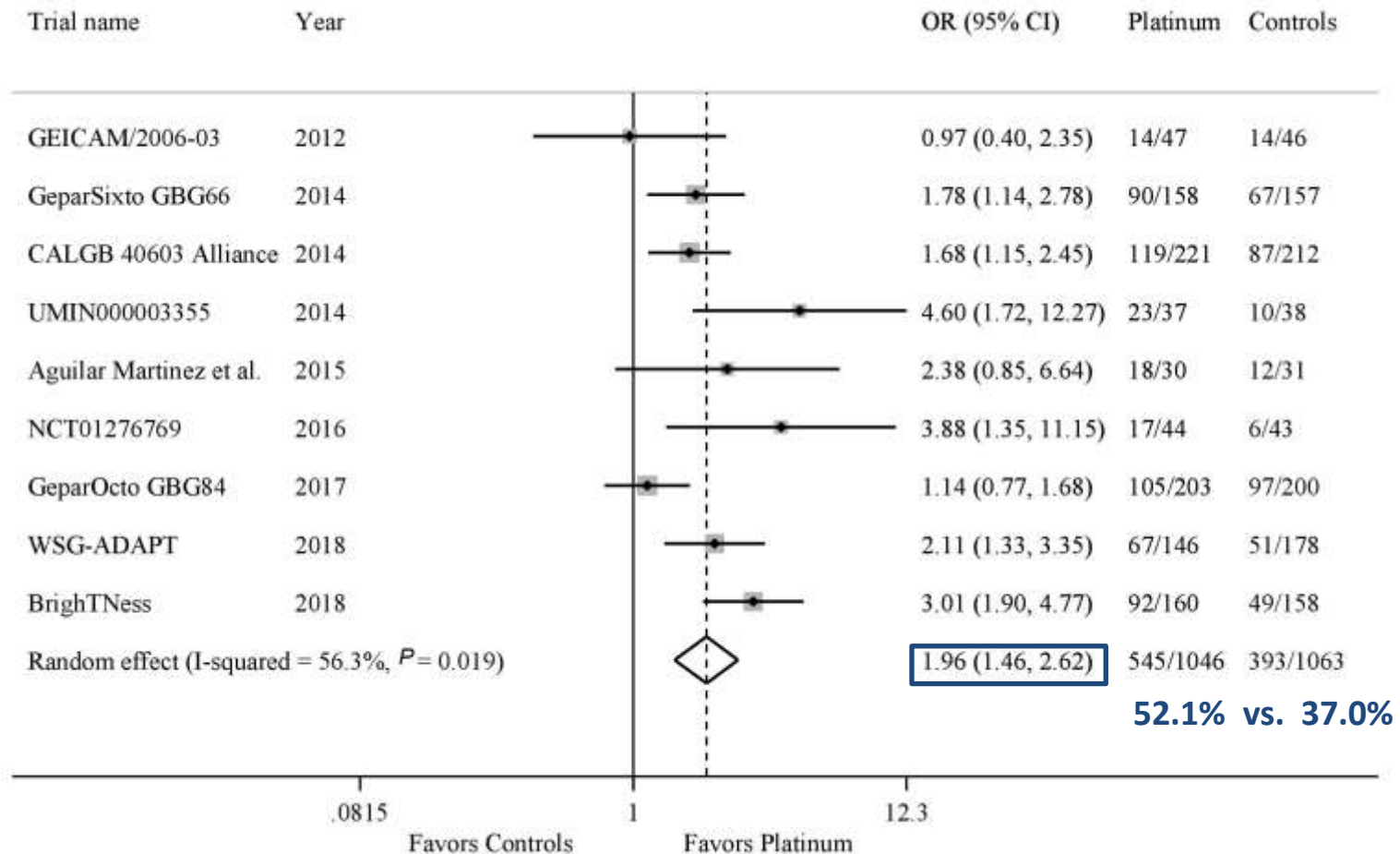
Results



Characteristics of the studies

Study	Study design	Treatment arms	TNBC patients, N
GEICAM/2006-03	Phase II	EC–DCb	47
		EC–D	46
GeparSixto GBG66	Phase II	P + Dox + Bev + Cb	158
		P + Dox + Bev	157
CALGB 40603 Alliance	Phase II	P + Cb ±Bev → ddAC	221
		P± Bev → ddAC	212
UMIN000003355	Phase II	PCb → CEF	37
		P → CEF	38
Aguilar Martinez	Phase II	Cis + P → Cis + Dox	30
		P → FAC	31
NCT01276769	Phase II	PCb	44
		EP	43
GeparOcto GBG84	Phase III	PDoxCb	203
		ddEPC	200
WSG-ADAPT	Phase II	Nab-P + Cb	146
		Nab-P + Gem	178
BrightNess	Phase III	P+Cb → AC	160
		P → AC	158

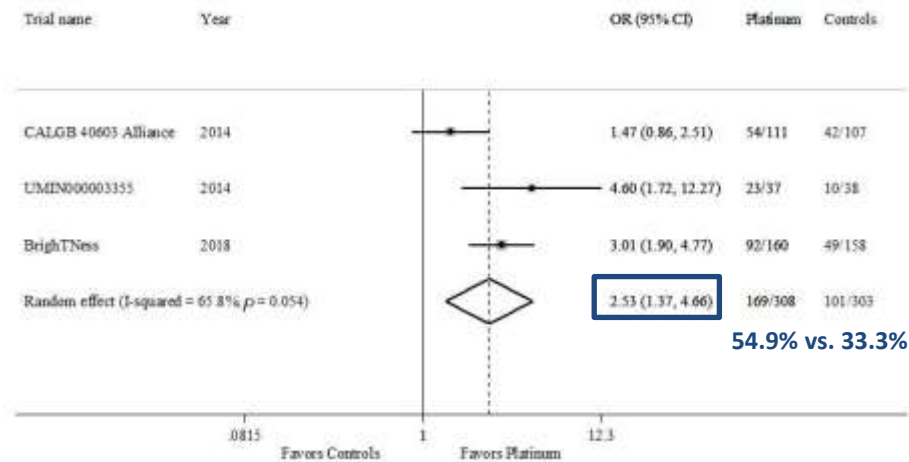
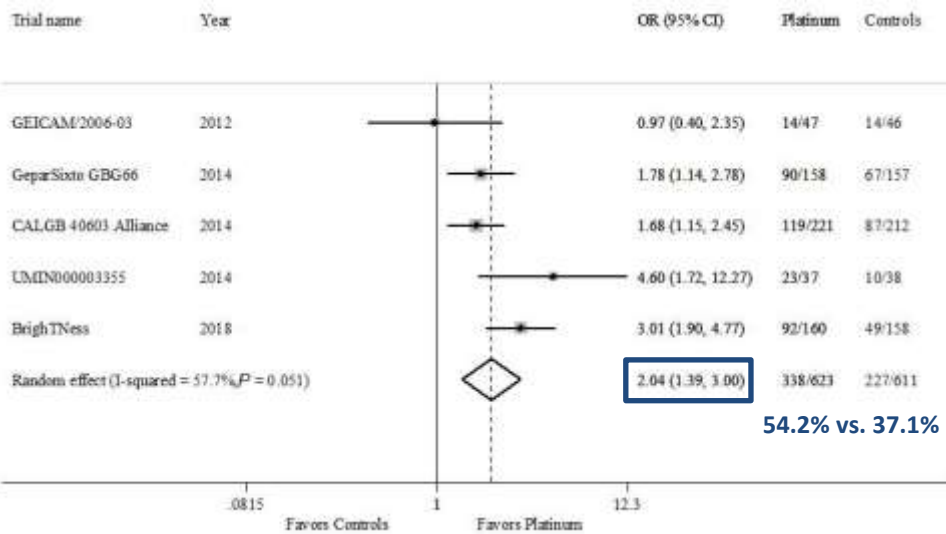
Results: pCR in all the studies



Results

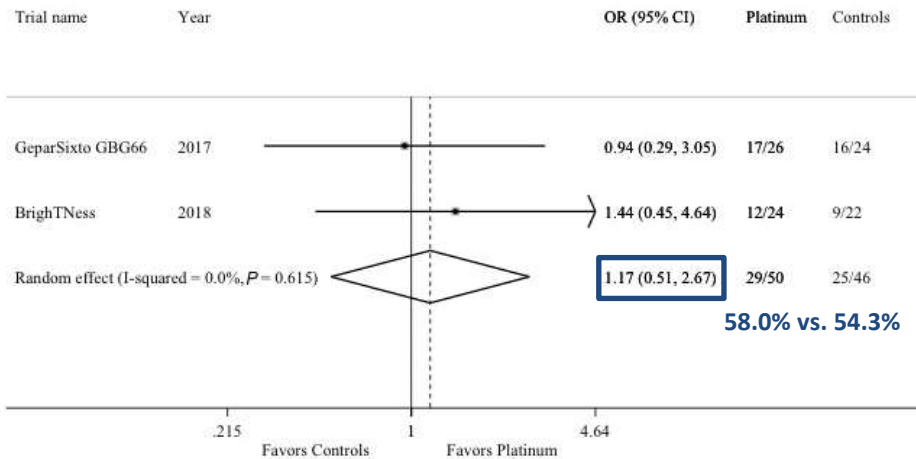
RCTs with the same CT backbone

RCTs with the same standard anthracycline- and taxane-based CT

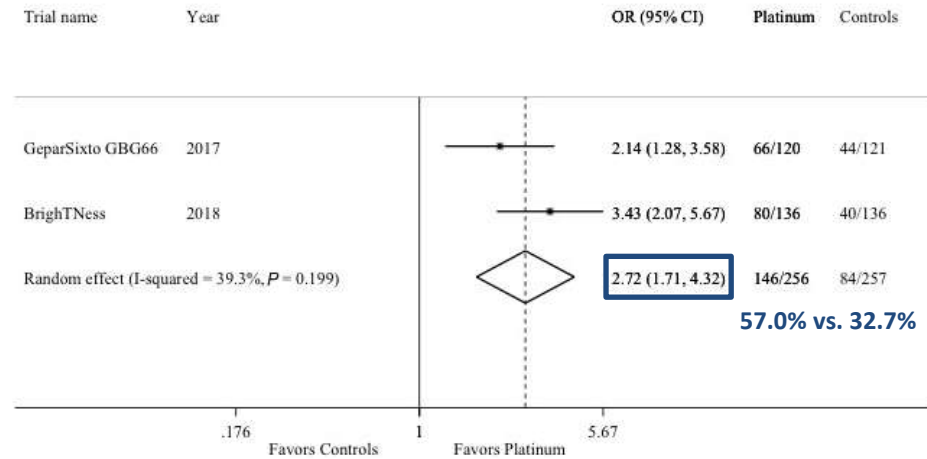


Results

BRCA-mutated patients

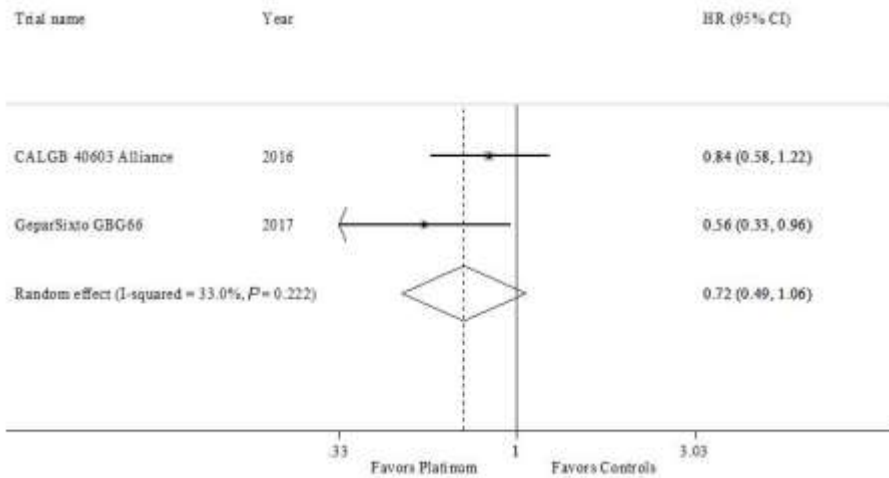


BRCA-negative patients

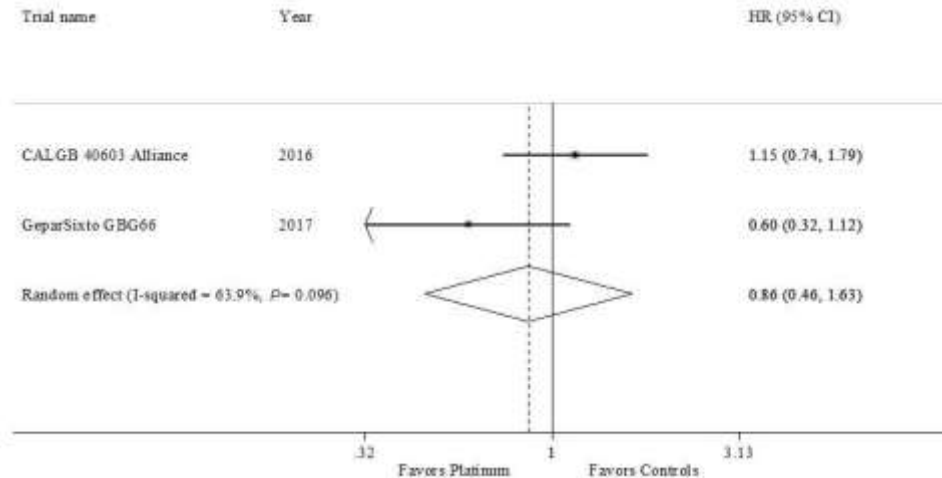


Results

Event-free survival

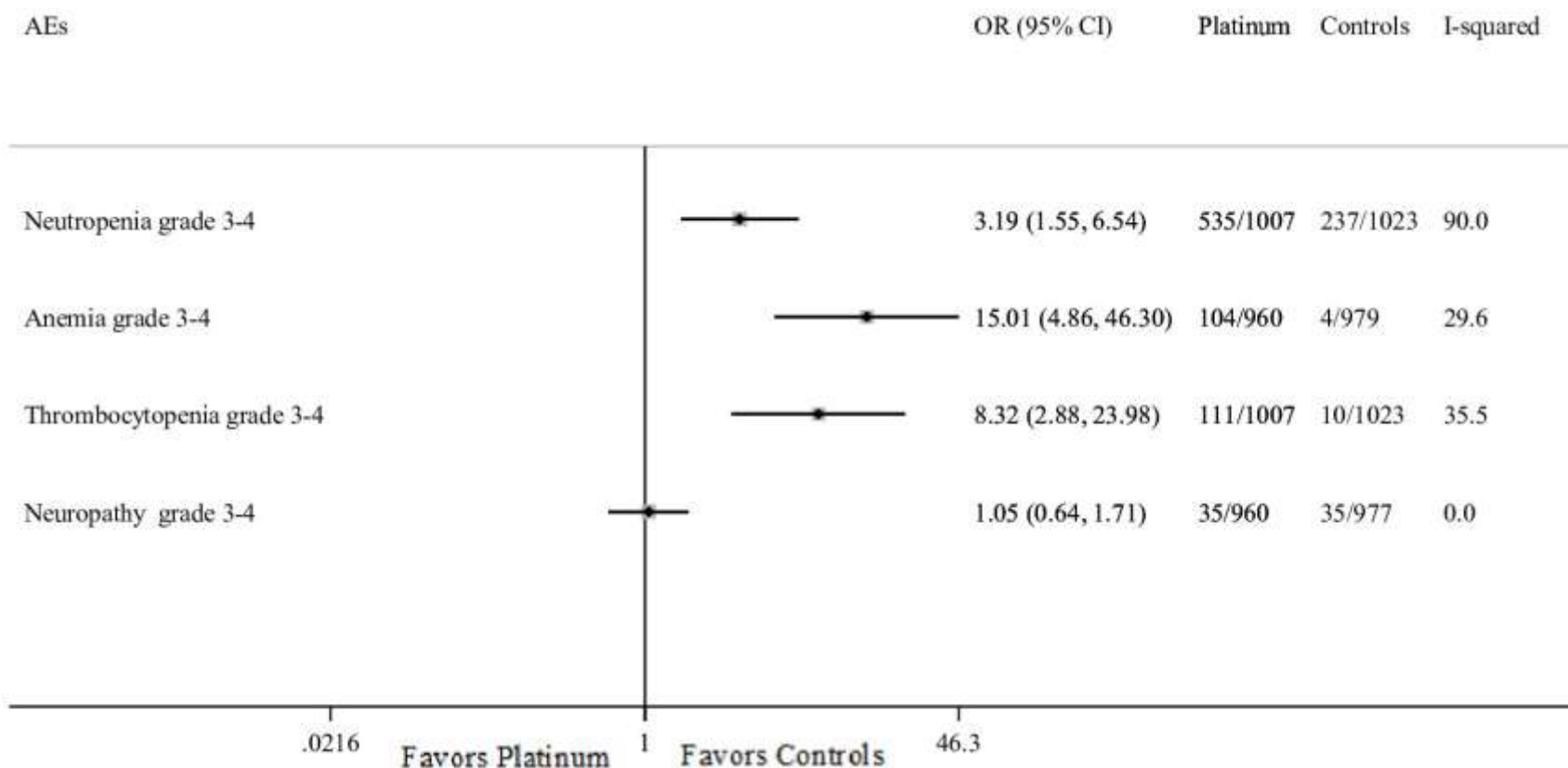


Overall survival



Results:

Safety profile overview



Conclusions

- Our meta-analysis showed that platinum-based neoadjuvant chemotherapy was associated with significant increased pCR rates in TNBC patients at the cost of worse hematological toxicity.
- The addition of platinum agents to standard anthracycline- and taxane-based neoadjuvant chemotherapy may be considered an option in unselected TNBC patients.

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