CARDIOVASCULAR ADVERSE EVENTS RELATED TO CDK4/6 INHIBITORS: A SYSTEMATIC REVIEW AND SAFETY META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION

In an era marked by the expanding indications of cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i):

- The standard first-line treatment for hormone receptor-positive, HER2-negative locally advanced and metastatic breast cancer (ABC).

- Their inclusion in adjuvant therapy strategies.

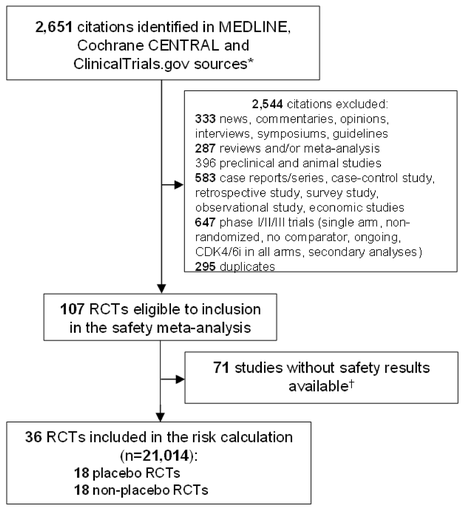
► It is essential to evaluate the associated risk of cardiovascular adverse events with CDK4/6i, supported by a high level of evidence.

METHODS

We **systematically reviewed phase 2 and 3 randomized controlled trials (RCTs)** comparing CdK4/6i versus control treatment (placebo and non-placebo) with available CVAEs in adults treated for a cancer **in** and up to April 6th, 2024. **ClinicalTrials.gov, MEDLINE and Cochrane.**

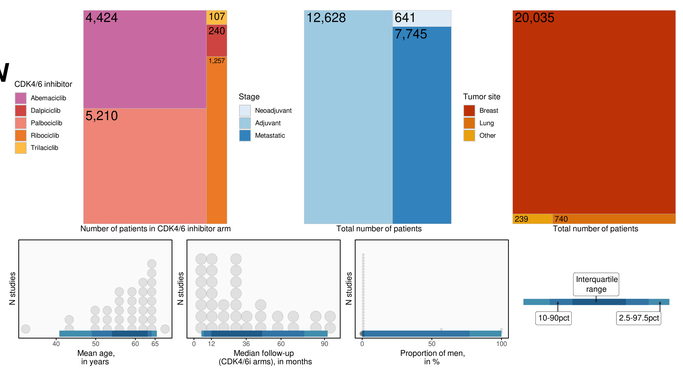
► **The primary outcome was the summary risk of 16 different CVAEs related to CdK4/6i versus any control,** using a random-effects meta-analysis to obtain Peto odds-ratios (Peto-ORs) with 95% confidence intervals (95%CIs) and logit transformation and inverse variance weighting to compute summary incidences.

► **Secondary outcomes included the summary risk of CVAEs in CDK4/6i group versus placebo**, the summary risk of serious CVAEs, subgroup analysis for each CVAE, according cancer localization, CDK4/6i type, cancer stage (localized or disseminated), menopausal status, previous line of treatment, bivariate meta-regression sex ratio, mean age, and median follow-up.

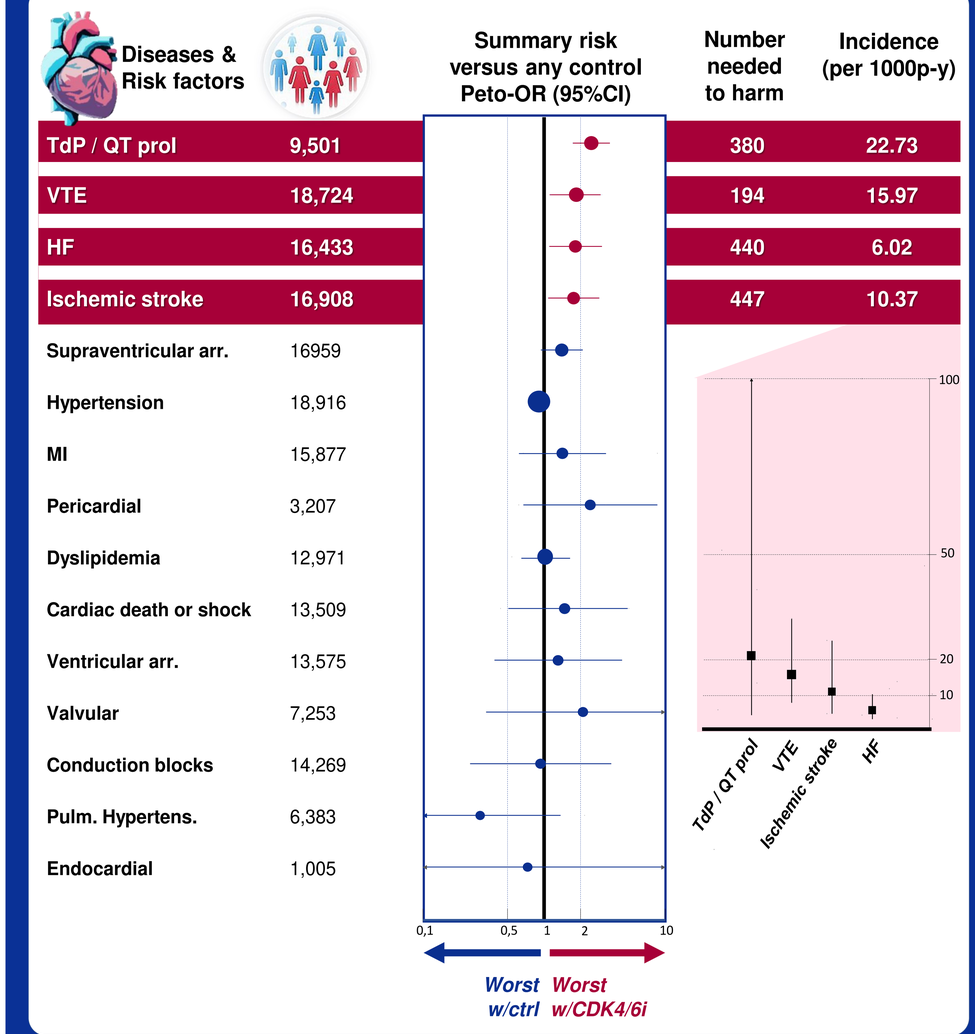


RESULTS

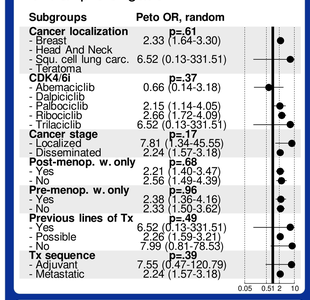
STUDY POPULATION

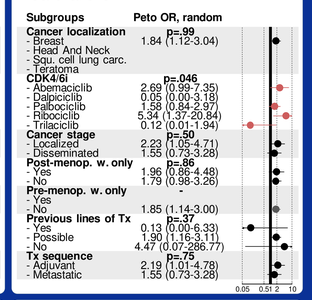


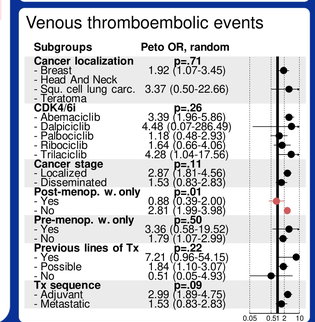
RESULTS

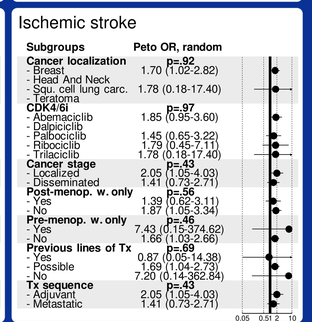


	Summary risk versus placebo Peto-OR (95% CI)
TdP / QT prolongation	2.24 (1.57-3.18)
Heart Failure	2.58 (1.05-6.35)
Venous thromboembolic events	1.78 (0.99-3.21)
Ischemic stroke	1.42 (0.66-3.05)









CONCLUSION

This meta-analysis highlights an increased risk of CVAEs associated with CdK4/6i, notably:

- **► TdP/QTprol, VTE, HF, and ischemic stroke.**
- **► Specifically, HF was significantly higher in ribociclib subgroup.**
- **► These findings should particularly alert clinicians considering the expanded indications for prescribing CDK4/6i.**