The Prognostic Value of PIK3CA Mutations in Neoadjuvant Anti-HER2 Therapy of Breast Cancer: A Meta-Analysis

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Main theme: Theme 4 – Cancer treatment & palliative care
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Title: The Prognostic Value of PIK3CA Mutations in Neoadjuvant Anti-HER2 Therapy of Breast Cancer: A Meta-Analysis
Abstract text: **Background:** The activation of downstream pathways such as PIK3CA mutation plays an important role in anti-HER2 resistance. However, researchers have failed to conclude the predictive value of PIK3CA mutation in HER2-positive breast cancer. Moreover, the update in anti-HER2 regimens and the lack of a recent large meta-analysis evaluating the association between PIK3CA mutations and the efficacy of anti-HER2 therapy led us to conduct more extensive research.
Aim: To assess the value of PIK3CA as a prognostic biomarker in anti-HER2 neoadjuvant therapy, we performed a meta-analysis of published studies that examined the correlation between PIK3CA mutations and the pathologic complete response (pCR) rate. We also estimated the role of PIK3CA mutations in patients treated with different anti-HER2 regimens to address the heterogeneity among therapeutic agents and to investigate the underlying mechanism of anti-HER2 resistance.
Methods: We searched PubMed, Web of Science, and Cochrane online databases for trials that compared PIK3CA wild-type and mutated patients who were treated with neoadjuvant anti-HER2 therapy, which included pCR as the primary outcome. Statistical analysis results were reported as risk ratios (RR), its 95% confidence intervals (CI), and the two-tailed P values, with the PIK3CA mutated (MT) group designated as experimental and the wild-type (WT) group as control.
Results: Fourteen studies were finally pooled into analysis, with a total of 1921 patients included. In the general population treated with anti-HER2 neoadjuvant therapy, PIK3CA mutations were associated with a significantly decreased pCR rate (RR=0.68; 95% CI:0.58-0.80; P<0.00001). Besides, PIK3CA MT were associated with lower pCR rate in patients treated with trastuzumab monotherapy (RR=0.71; 95% CI: 0.54-0.94; P=0.02) or trastuzumab plus pertuzumab (RR=0.72; 95% CI: 0.53-0.99; P=0.04). However, the MT and WT group demonstrated no significant difference in pCR rate in patients who received trastuzumab plus lapatinib (RR=0.67; 95%CI: 0.34-1.32; P=0.25) or lapatinib monotherapy (RR=0.82; 95% CI:0.43-1.54; P=0.53).
Conclusion: PIK3CA mutations significantly reduced the benefit of neoadjuvant anti-HER2 therapy, with a more pronounced impact on trastuzumab-containing regimens.

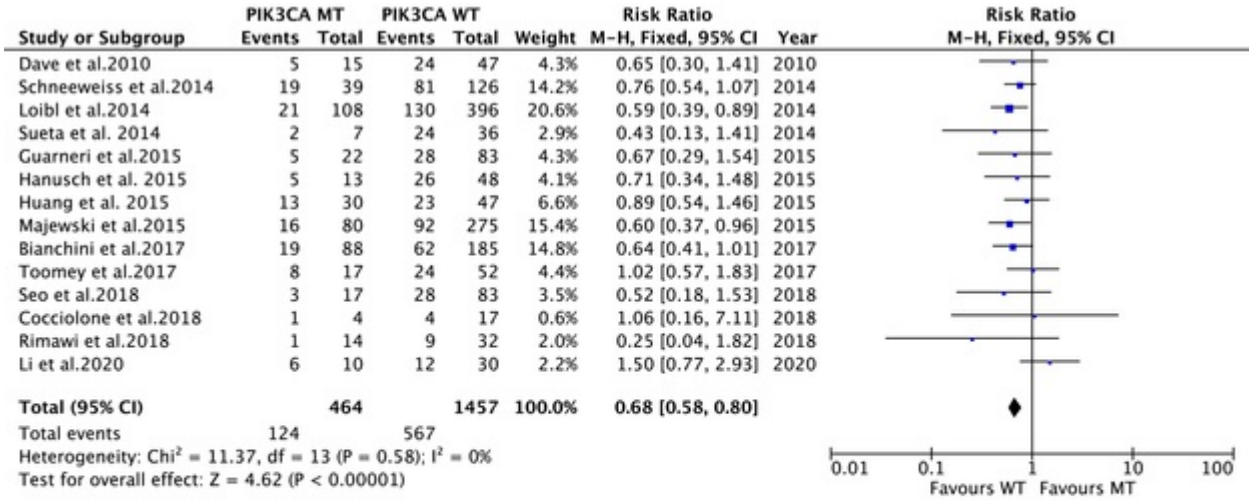

Figure 1. Forest plot for corelation between PIK3CA mutations and pathologic complete response rates of neoadjuvant anti-HER2 therapy (fixed-effect model). MT: mutated-type. WT: wild-type.

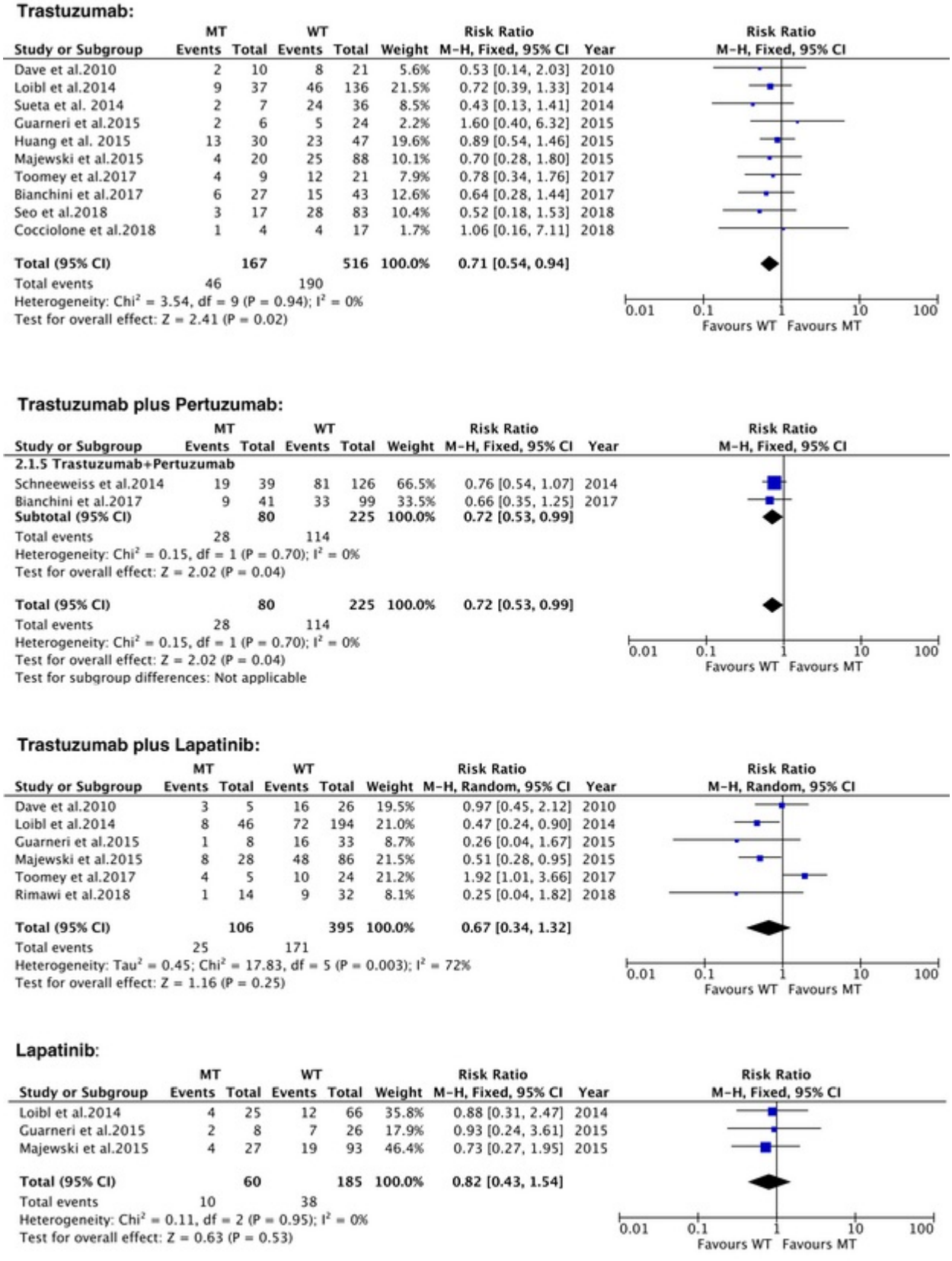

Figure 2. Forest plots for corelation between PIK3CA mutations and pathologic complete response rates of neoadjuvant anti-HER2 therapy specified by anti-HER2 regimens. MT: mutated-type. WT: wild-type.

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