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Editorial

Firm Evidence of Neoadjuvant Bevacizumab Plus Chemotherapy Versus Chemotherapy Alone to Treat Non-Metastatic Breast Cancer: A Trial Sequential Analysis

Hong Weng*

Center of Evidence Based and Translational Medicine, Zhongnan Hospital of Wuhan University, Chin

***Corresponding author**

Hong Weng, Center of Evidence Based and Translational Medicine, No. 169 Donghu Road, Wuchang District, Wuhan, Hubei Province, China, Tel: 8602767812817; Fax: 86 027 67812817; Email: wengh92@163.com

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EDITORIAL

I read with great interest a meta-analysis by Cao et al., [1] published in Plos One entitled 'Neoadjuvant Bevacizumab plus Chemotherapy versus Chemotherapy Alone to treat Non-Metastatic Breast Cancer: a Meta-Analysis of Randomised Controlled Trials'. The authors of the meta-analysis concluded that higher proportions of patients achieved pathological complete response (pCR) when bevacizumab was added to neoadjuvant chemotherapy compared with when they received chemotherapy alone. As our team previously described that random error commonly occurred in results of meta-analyses due to limited quantity of included trials and limited sample size [2]. Therefore, the reliability of the effects of neoadjuvant bevacizumab plus chemotherapy versus chemotherapy alone to treat non-metastatic breast cancer remains unclear. In order to well acknowledge the evidence of the effects of neoadjuvant bevacizumab plus chemotherapy in treating with non-metastatic breast cancer, I performed a trial sequential analysis regarded on the pCR and total pCR (tpCR) based on the previous meta-

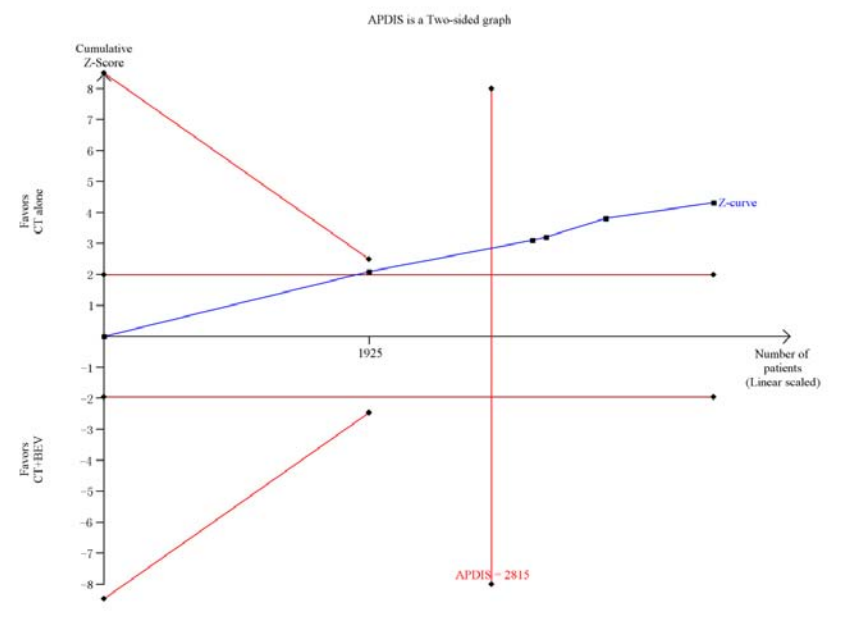

Figure 1 Trial sequential analysis of pCR.

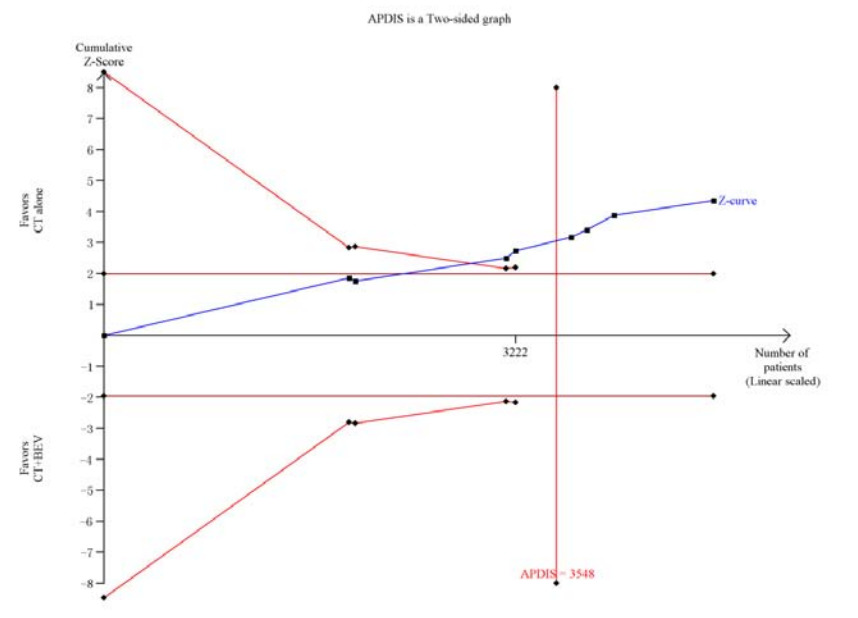

Figure 2 Trial sequential analysis of tpCR.

analysis conducted by Cao et al. [1].

The trial sequential analysis was performed using a priori diversity-adjusted information size (APDIS) with $\alpha = 0.05$, $\beta = 0.9$ (power at 90%), 20% of an appropriate anticipated intervention effect of relative risk reduction, and proportion of event in controls obtained from the results of meta-analysis (25.8% for pCR and 21.5% for tpCR). Cao and colleagues [1] calculated odds ratio and 95% confidence interval (CI) as effect measurement. In order to perform trial sequential analysis, we recalculated the relative risk (RR) and corresponding 95% CI to assess the intervention effect. Significance level was $\alpha = 0.05$. The statistical analysis was performed using TSA software version 0.9 beta.

The meta-analysis of pCR showed a statistical significance between neoadjuvant bevacizumab plus chemotherapy versus chemotherapy alone (RR = 1.22, 95% CI 1.12 to 1.34; $I^2=0$). The trial sequential analysis of pCR showed that the 4426 (157.2%) of the 2815 APDIS was accrued (Figure 1). The cumulative z-curve crossed the conventional boundary and reached the APDIS providing firm evidence of increased pCR in non-metastatic breast cancer patients treated with neoadjuvant bevacizumab plus chemotherapy compared with chemotherapy alone.

The meta-analysis of tpCR also showed a statistical significance between neoadjuvant bevacizumab plus chemotherapy versus chemotherapy alone (RR = 1.25, 95% CI 1.13 to 1.38; $I^2=0$). The trial sequential analysis of pCR showed that the 4776 (134.6%) of the 3548 APDIS was accrued (Figure 2). The cumulative z-curve crossed the conventional boundary and reached the APDIS providing firm evidence of increased pCR in non-metastatic breast cancer patients treated with neoadjuvant bevacizumab plus chemotherapy compared with chemotherapy alone.

In conclusion, the results of trial sequential analyses confirmed the increased pCR and tpCR in non-metastatic breast cancer patients treated with neoadjuvant bevacizumab plus chemotherapy compared with chemotherapy alone.

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