Severe cardiac events following treatment with trastuzumab in women with breast cancer: a meta-analysis of clinical trials and cohort studies

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Trastuzumab is associated with prolonged survival in women with HER2-positive breast cancer, but it may increase the risk of heart disease[1,2]. However, the occurrence of severe cardiotoxicity in real-life settings has not been determined. The present analysis was aimed at estimating the frequency of severe cardiac adverse events (i.e., myocardial infarct, grade III-IV heart failure, left ventricular ejection fraction ≤ 40%, or cardiac events leading to hospitalization) up to three years after trastuzumab initiation. We searched MEDLINE, EMBASE and the Cochrane Library (1996 to January 2014). Eligible studies were clinical trials and cohort studies that reported the frequency of cardiotoxicity regardless of drug dose, treatment regimen, or follow-up length, with the exception of the combination of target therapies. A meta-analysis was performed to calculate the weighted summary proportion of severe cardiac events and the respective 95% confidence intervals (CIs) using a random-effects model. We screened 3,826 abstracts for eligibility and included 58 studies (29,598 patients). Severe cardiac adverse events occurred in 3.00% (95%CI, 2.41-3.64), 2.62% (95%CI, 1.97-3.35) and 3.14% (95%CI, 2.12-4.37) of overall, early (EBC) and metastatic (MBC) breast cancer patients, respectively. In EBC, the proportion increased from 2.40% in the first-year to a plateau of 3.17% in the second year and 2.95%, in the third year. In MBC, the proportion increased from 3.00% to 3.68% when trastuzumab was used as first-line or further-lines of therapy, respectively. In EBC, cardiotoxicity occurred in 2.90% of patients treated with taxanes and anthracyclines, as compared to 0.92% in patients treated with taxanes without anthracyclines. The occurrence of cardiotoxicity varied according to age, increasing from 2.31% in individuals <50 years, to 3.46% in those aged 50-59 years, to 4.91% in those with >60 years of age. Cardiotoxicity was higher in smokers (5.3%), patients with dyslipidemia (3.9%), body mass index ≥25 (6.5%), diabetes (6.2%), hypertension (5.5%), or positive history of cardiac disease (19.1%). Clinical trials consistently reported lower cardiac toxicity rates than observational studies for women with either EBC (1.7% vs 3.2%) or MBC (2.8% vs 4.4%). In conclusion, following the initiation of therapy with trastuzumab, approximately 3 out of 100 patients develop severe cardiotoxicity after two years. Despite the benefits of trastuzumab in terms of life prolongation are well established, these should be weighed against the risk of severe cardiotoxicity, which may result in a serious detriment to the quality of life, particularly in elderly patients and those with cardiovascular risk factors.

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