



Title **The Clinical Effectiveness of Trastuzumab for Breast Cancer**

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Aim

To evaluate the effectiveness of trastuzumab in managing breast cancer.

Conclusions and results

One RCT of trastuzumab plus chemotherapy (cyclophosphamide plus anthracycline or paclitaxel) versus chemotherapy alone. Study population included women with HER2-overexpressing metastatic breast cancer (MBC) at level 2+ or 3+ who had not received prior treatment for MBC. Overall quality of the trial considered to be good. Trastuzumab administered for the duration of the trial in weekly infusions as long as the treatment was considered to be beneficial. Addition of trastuzumab to chemotherapy resulted in significantly less disease progression and treatment failure, longer progression-free survival, and greater complete and overall tumor response when compared to chemotherapy alone. A significantly greater incidence of congestive heart failure was reported among those receiving trastuzumab plus chemotherapy compared to those on chemotherapy alone. The incidence seemed to be highest with trastuzumab plus anthracycline, rather than with trastuzumab plus paclitaxel.

No RCTs found that met the initial inclusion criteria for trastuzumab used as monotherapy. Hence, this section is based on noncomparative Phase II studies. The overall quality of these studies according to the checklist for case series was found to be moderate. Trastuzumab monotherapy was shown to have some antitumor effects in terms of overall tumor response (partial and complete), which ranged from 12% to 24% in the three studies. An independent response committee assessed tumor response outcomes in two studies, whereas tumor response was assessed by the investigators in the third study. Similar durations of tumor response were reported by two studies of 9 and 9.1 months.

One study reported the number of complete (five (3%)) or partial (26 (15%)) tumor responses for participants with tumors overexpressing HER2 at level 3+. In another study, the overall tumor response rate for this group of participants was reported for both treatment groups combined as 31% (26/85). These results demonstrated that most tumor responses occurred in participants with tumors overexpressing HER2 at level 3+.

Trastuzumab when used in combination with chemotherapy seemed to be more effective than chemotherapy alone for treatment of MBC overexpressing HER2 at level 3+ in individuals who had not received prior treatment for MBC. However, it seemed to be associated with congestive heart failure, particularly in patients that received anthracycline-based chemotherapy.

- Trastuzumab monotherapy when used as second-line or subsequent therapy for the treatment of MBC overexpressing HER2 at level 3+ appeared to have some antitumor effects in terms of overall tumor response based on noncomparative studies (which provide relatively weak evidence) of moderate quality.

Recommendations

Further large, well-conducted RCTs are required to provide more evidence of the effectiveness of trastuzumab when used within its licensed indications, in addition to other indications.



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Methods

Only randomized controlled trials (RCTs) were initially considered for inclusion. Included trials had to evaluate trastuzumab alone or in combination with other agents vs systemic therapy without trastuzumab, and had to include individuals with breast cancer. No RCTs of trastuzumab used as monotherapy for treating breast cancer were found. The National Institute for Clinical Excellence (NICE), therefore, requested that noncomparative Phase II studies of trastuzumab used as monotherapy for the treatment of HER2-overexpressing (at level 3+) breast cancer be evaluated for inclusion in the review, and these data have subsequently been added. Several databases were searched using strategies designed specifically for each database. Additional references were identified through reviewing manufacturer and sponsor submissions made to NICE, the bibliographies of retrieved articles, conference proceedings, and by searching the Internet.

Further research/reviews required

Further large, well-conducted RCTs are required to provide more evidence of the effectiveness of trastuzumab when used within its licensed indications, in addition to other indications.