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Title Trastuzumab as an Adjuvant Therapy for Early Breast Cancer and Economic Evaluation

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http://www.moh.gov.my/index.php/database_stores/store_view_page/30/298

Aim

To assess the safety, efficacy/effectiveness and cost-effectiveness of trastuzumab as an adjunct in early breast cancer patients either concurrently or sequentially to chemotherapy.

Conclusions and results:

Part 1: Systematic review of literature - Safety

There was high level of evidence to suggest that the risk of CHF was significantly higher in patients treated with trastuzumab compared to non-trastuzumab control group (RR 5.11; 90% CI: 3.00, 8.72, p<0.00001) in one Cochrane review, (RR 3.19; 95% CI: 2.03, 5.02, p<0.00001) in one systematic review and meta-analysis. Evidence also suggest that the risk was significantly higher with longer duration of treatment (> 6 months) RR 5.39; 90% CI: 3.56, 8.17, P<0.00001 and also with higher loading dose of treatment (8mg/kg) RR 6.79; 95% CI: 2.03, 22.73, p<0.00001.

Effectiveness

The overall survival (OS) significantly favoured trastuzumab containing regimen over non-trastuzumab control group, (HR 0.66; 95% CI: 0.55, 0.77, p<0.00001). In terms of duration, subgroup analysis reported that the OS significantly favoured trastuzumab containing regimen over non-trastuzumab control group trials where trastuzumab was given longer (> 6 months), HR 0.67; 95% CI: 0.57, 0.80, P<0.00001. In the trials that gave trastuzumab and chemotherapy concurrently, HR significantly favoured trastuzumab-containing regimens (HR 0.64; 95% CI: 0.57, 0.80, P<0.00001).

Disease free survival (DFS) favoured trastuzumab containing regimen over non-trastuzumab control group (HR 0.60; 95% CI: 0.50, 0.71, P<0.00001). In terms of duration of treatment, there was no significant difference in DFS when trastuzumab was used for less than six months, or more than six months. The DFS significantly favoured trastuzumab containing regimen over non-trastuzumab control group when used either concurrently or sequentially. Limited evidence to suggest that two years duration of adjuvant trastuzumab was not more effective that one year of treatment. However, six months treatment with trastuzumab failed to show that it was non-inferior to twelve months of trastuzumab. Despite the higher rates of cardiac events, twelve months of adjuvant trastuzumab should remain the standard of care.

Cost/Cost-effectiveness

A wide range of ICER/QALY reported: ranging from USD 7,676 to USD 71,491.

Part 2: Economic evaluation

From the decision analytic modelling that has been conducted, addition of 1-year treatment with trastuzumab on top of standard adjuvant chemotherapy is considered as a cost-effective strategy for early breast cancer with HER2 positive, yielding an ICER of RM 83,544.59 per QALY gained. This is within the suggested value of cost-effectiveness threshold by WHO (1-3 times GDP per capita). However, if suggested cost-effectiveness threshold for Malaysia is taken into consideration which is ≤1 GDP per capita, this treatment may not be a cost-effective strategy. Based on one-way sensitivity analysis performed, these components have shown to be a sensitive parameter for ICER determination: discount rate, disease-free state utility values, route of trastuzumab administration and cost of trastuzumab.

Recommendations (if any)

The use of trastuzumab in early stage HER2 positive breast cancer is recommended. However, it will be more cost-effective and affordable with the drug price reduction and changing route of administration (From IV to SC).

Methods

The following electronic databases were searched via OVID Interface: MEDLINE (1946 to present), EBM Reviews-Cochrane Database of Systematic Reviews (2005 to Jun 2016), EBM Reviews-Cochrane Central Register of Controlled Trials (Jun 2016), EBM Reviews–Database of Abstracts of Review of Effects (2nd Quarter 2016), EBM Reviews-Health Technology Assessment (2nd Quarter 2016) NHS economic evaluation database (2nd Quarter 2016), PubMed and INAHTA database. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles.

Further research/reviews required

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