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**ORIGINAL ARTICLE**

# Modelling the cost-effectiveness of adjuvant lapatinib for early-stage breast cancer

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**Abstract**

*Background.* It has been shown in the NeoALTTO trial that a neoadjuvant regimen containing paclitaxel, lapatinib and trastuzumab is superior to regimens which include only one of the HER2 antagonists with paclitaxel. In light of these results, we modelled the potential cost-effectiveness of adjuvant lapatinib for patients with HER2-positive early-stage breast cancer. *Material and methods.* We constructed a Markov state-transition model with three different health states: disease free, relapse, and death. We assumed an 18-week course of lapatinib was added to the TCH arm of the BCIRG 006 trial. Since no efficacy data are available for combining adjuvant lapatinib with trastuzumab, we ran the model assuming five different hypothetical hazard ratios for disease free survival when lapatinib is added to TCH (TCH was used as the control group). The hazard ratios were 0.9, 0.8, 0.7, 0.6, and 0.5. Outcomes are given in quality-adjusted life-years (QALYs). Both costs and QALYs were discounted at the 4% rate. We calculated the cost per QALY from the perspective of the Irish health care system. Probabilistic sensitivity analysis and one-way sensitivity were performed and confidence intervals were bootstrapped. *Results.* The incremental cost-effectiveness ratios (ICERs) for the five hazard ratios are €53 089/QALY, €27 893/QALY, €18 463/QALY, €13 527/QALY and €10 490/QALY, respectively. Using the €45 000/QALY threshold, an adjuvant lapatinib regimen is cost-effective at the 0.8 hazard ratio. Adjuvant lapatinib becomes cost-effective at the 0.879 hazard ratio where the ICER is €44 825/QALY. *Conclusion.* In the Irish setting, an adjuvant lapatinib regimen would be considered cost-effective for patients with HER2-positive early-stage breast cancer for four of the five hypothesised hazard ratios. Data from both adjuvant and neoadjuvant trials suggest that the hazard ratio required to achieve cost-effectiveness for adjuvant lapatinib is both possible and plausible.

Alterations in the human epidermal growth factor receptor (HER2) gene, usually amplification, occur in 20% of breast cancers and are associated with inferior prognosis compared to HER2 normal breast cancer. Treatment with trastuzumab (Herceptin; Roche, Switzerland), a humanised monoclonal antibody directed against the protein product of the HER2 gene has been shown to increase objective response in patients with both metastatic and primary HER2 altered breast cancer, and to prolong survival in both the metastatic and adjuvant settings [1,2]. Lapatinib (Tykerb; GlaxoSmithKline, UK) is a newer HER2 antagonist which works by a different mechanism. It is a tyrosine kinase inhibitor which targets both HER2 and EGFR, (HER1). Lapatinib works by inhibiting the receptors and causes apoptosis or growth arrest in tumour cells. While it is currently licensed as treatment for metastatic HER2-positive breast cancer following failure of trastuzumab therapy, laboratory data suggest a potential role in combination with trastuzumab. Data supporting this hypothesis are now available for the pre-operative treatment of earlier stage disease.

Results from the NeoALTTO trial show that a "neoadjuvant" regimen of lapatinib, trastuzumab and paclitaxel produced a pathological complete response (pCR) rate of 51.3% compared to 29.5% and 24.7% for regimens containing only trastuzumab or lapatinib, respectively with paclitaxel [3]. There are as yet no survival data for this trial, but it does tend to support the hypothesis that dual inhibition of HER2 might be a valid approach to the treatment of HER2-positive breast cancer in the neoadjuvant setting. Given the generally positive correlation

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between pCR rates and disease free survival (DFS) rates, and the known therapeutic equivalence between pre-operative and adjuvant administration of the same systemic regimens, it is plausible that an adjuvant regimen containing both lapatinib and trastuzumab might be superior to one with trastuzumab alone [4].

In light of these results, we have modelled the hypothetical cost-effectiveness of an adjuvant treatment regimen, which contains both lapatinib and trastuzumab, for patients with HER2-positive early-stage breast cancer.

## Material and methods

### *Design and structure of the model*

We constructed a Markov model using TreeAge Pro Suite 2013 (TreeAge Software Inc., Williamstown, MA, USA) to analyse the cost-effectiveness of a novel adjuvant lapatinib regimen compared to the standard trastuzumab treatment for patients with HER2-positive early-stage breast cancer. In the model, presented in Figure 1, the patients move between the following three health states: disease free, relapse and death. Movements between health states are based on transition probabilities which are calculated from clinical trials. Each period consists of three months. Patients accumulate both costs and quality-adjusted life-years (QALYs) for each period spent in a particular health state. We discount both the costs and QALYs at a 4% rate. The results are presented in incremental cost-effectiveness ratios (ICERs) in terms of cost per QALY gained. To perform probabilistic sensitivity analysis (PSA), we simulated the model using second order Monte Carlo analysis (1000 simulations) and constructed confidence intervals with bootstrap replications (1000 replications). In addition, we also conducted one-way sensitivity analysis on selected hazard ratios.

### *Patients and treatment plans*

The patients in our model are assumed to be clinically similar to the patients treated in the BCIRG 006 study: patients have HER2-positive early-stage breast cancer, the median patient age is 50, they have undergone some combination of surgery, radiotherapy and hormonotherapy and they are now ready for adjuvant therapy [2]. We compare two adjuvant treatment regimens in this model: The standard TCH arm from BCIRG 006 and a novel regimen consisting of TCH plus lapatinib.

In a TCH regimen, patients receive 75 mg/m$^2$ of docetaxel and 6 mg per ml/min of carboplatin (area under the curve) once every three weeks for six cycles. Trastuzumab is given concurrently with this treatment and consists of a 4 mg/kg loading dose followed by 2 mg/kg weekly for 12 weeks. After this, the dosage becomes 6 mg/kg once every three weeks until a one-year course is completed. The BCRIG 006 study provides efficacy data for TCH for up to five years. After this, trastuzumab is assumed to have no benefit. Due to the lack of long-term data on the efficacy of trastuzumab, we use data from the Early Breast Cancer Trial Collaborative Group meta-analysis to obtain information on the 15-year relapse rates for patients undergoing anthracycline-based chemotherapy [5]. As patients who undergo trastuzumab treatment are at risk of cardiotoxicity, we include the cost of four echocardiograms (echo) and cardiologist reports. Patients who develop asymptomatic cardiotoxicity (decrease in left ventricle ejection fraction) are treated with a course of angiotensin converting enzymes (ACE) inhibitors and another echo. Patients who experience symptomatic cardiotoxicity (congestive heart failure) are treated with ACE inhibitors, beta blockers and another echo [6,7].

We compare this regimen to one consisting of TCH plus lapatinib. Lapatinib is given concurrently with trastuzumab at a dose of 1000 mg a day for 18 weeks, based on the regimen in the NeoALTTO study. The main side effect associated with lapatinib is grade III/IV diarrhoea which occurs in 21.1% of cases [3]. Treatment includes octreotide, ciprofloxacin and a stay in hospital [8].

For patients who relapse, treatment involves a combination of capecitabine and trastuzumab based on the GBG 26/BIG 03-05 trial. Patients receive the median nine cycles of capecitabine and trastuzumab

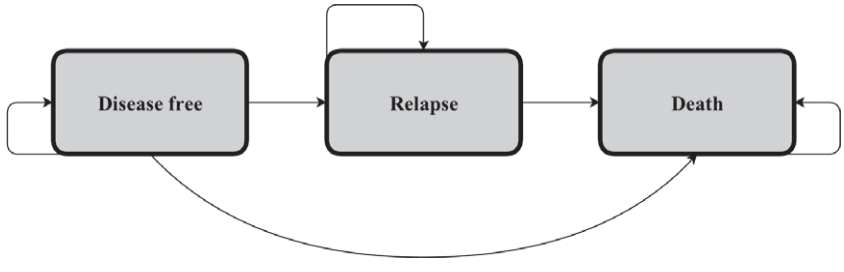


Figure 1. The Markov model.

and the median overall survival is 24.9 months [9,10]. Before patients transition to the death state, we assume they undergo end of life or palliative care. Finally, we use data from Irish life tables to allow patients to die from any cause during the model [11]. The rates are then adjusted in accordance with the patients' age.

*Model inputs for transition probabilities*

Transition probabilities, sourced from clinical trials, are given in Table I. All the hazard and survival rates were converted into transition probabilities for three-month time periods.

The main difficulty with this model is that the transition probability from disease free to relapse, for an adjuvant regimen with lapatinib, is unknown. Unfortunately, no clinical trial has published results which detail the hazard ratio for DFS for the addition of lapatinib to the trastuzumab for early-stage breast cancer. The NeoALTTO trial, however, shows that lapatinib in combination with the trastuzumab, leads to a higher pCR rate than trastuzumab alone. Since pCR rates have been shown to be positively correlated with survival, a hazard ratio for adjuvant lapatinib would be some unknown value that is $<1$. To overcome this problem, we run the model for a number of possible hazard ratios; 0.9, 0.8, 0.7, 0.6

Table I. Inputs for the Markov model.

| | Value | Distribution | Parameter | Range[a] | Source |
|---|---|---|---|---|---|
| Probability | | | | | |
| Disease free to disease free, years 1–3 | 0.9873 | Beta | $\alpha = 7817.06$, $\beta = 100.79$ | CI | 2 |
| Disease free to disease free, years 4–5 | 0.9933 | Beta | $\alpha = 11\,995.77$, $\beta = 81.10$ | CI | 2 |
| Disease free to disease free, years 6–15 | 0.9897 | Beta | $\alpha = 206\,421.83$, $\beta = 2155.02$ | CI | 6 |
| Disease free to disease free, years 15+ | 0.9948[b] | Beta | $\alpha = 206\,421.83$, $\beta = 2155.02$ | CI | 6 |
| Relapse to relapse, years 1–2.5[c] | 0.9740 | Beta | $\alpha = 1074.13$, $\beta = 28.67$ | CI | 10 |
| Relapse to relapse, years 2.5+ | 0.8750 | Beta | $\alpha = 41.10$, $\beta = 5.87$ | CI | 10 |
| Cardiotoxicity during treatment (in year 1) | 0.0980 | – | – | – | 2 |
| Asymptomatic cardiotoxicity | 0.7800 | – | – | – | 24 |
| Diarrhoea during treatment (in year 1) | 0.2110 | – | – | – | 4 |
| Utility | | | | | |
| Current health | 0.9330 | Beta | $\alpha = 11.32$, $\beta = 0.81$ | CI | 15 |
| Disease free | 0.9890 | Beta | $\alpha = 106.60$, $\beta = 1.19$ | CI | 15 |
| Relapse | 0.7100 | Beta | $\alpha = 1.56$, $\beta = 0.64$ | CI | 15 |
| Cost (€2011) | | | | | |
| Carboplatin | €660.00 | Normal[d] | SD = 66.00 | ±20% | e |
| Docetaxel | €8328.71 | Normal | SD = 832.87 | ±20% | e |
| Trastuzumab (early-stage) | €40 973.40 | Normal | SD = 4097.34 | ±20% | e |
| Four echoes and cardiologist reports | €1068.00 | Normal | SD = 106.8 | ±20% | f |
| Lapatinib | €9933.84 | Normal | SD = 993.38 | ±20% | e |
| Capecitabine | €3913.87 | Normal | SD = 391.38 | ±20% | e |
| Trastuzumab (relapse) | €21 302.64 | Normal | SD = 2130.26 | ±20% | e |
| Asymptomatic cardiotoxicity | €321.00 | Normal | SD = 32.10 | ±20% | e |
| Symptomatic cardiotoxicity | €348.00 | Normal | SD = 34.80 | ±20% | e |
| Diarrhoea | €753.60 | Normal | SD = 75.36 | ±20% | e |
| Palliative care | €13 500.00 | Normal | SD = 1350.00 | ±20% | e |

CI, confidence interval; SD, standard deviation.

[a] This is the range which is used to develop the parameters of the distribution and in which the mean value is allowed to vary in probabilistic sensitivity analysis; [b] Since no data exist on the recurrence rates of patients after 15 years we adopt the same approach as Kurian et al. [25] and half the probability of relapse from the previous probability; [c] Because patients in this trial were older than the patients in BCIRG 006 (median age 52.5) we extended the transition probability from 1 year to 2.5 years to take into account the fact that patients in our model are slightly younger; [d] While gamma distribution are often used to model costs we use the normal distribution since specifying a standard deviation of 10% of the mean allows us the vary the costs between 20% in probabilistic sensitivity analysis; [e] St. Vincent's Hospital, personal communication; [f] Bon Secours Hospital, personal communication.

and 0.5. A similar method has been used previously by Norum et al. when they tested the cost-effectiveness of adjuvant trastuzumab by using improvements in distant relapse free survival as a surrogate for 10% and 20% improvements in overall survival, and by Dedes et al., when they investigated the cost-effectiveness of adjuvant trastuzumab over different time periods [12,13]. We assume these hazard ratios for disease free survival correspond to a five-year period, like the BCIRG 006 data for trastuzumab. After this, lapatinib, again like trastuzumab, is assumed to have no benefit.

*Model inputs for effectiveness*

The utilities that are used in the model are presented in Table I. Values for the utility associated with health states are taken from a study by Mansel et al. [14]. These utilities were chosen because of the similarities in setting (a British cost-effectiveness study of hormonal adjuvant treatment for early-stage breast cancer) and the detailed description of how they were derived (a chained standard gamble approach).

*Model inputs for costs*

The costs of treatments used in both arms are also presented in Table I. All the drug costs come from the pharmacy in St. Vincent's Hospital, Dublin. Costs for echocardiogram and cardiologist come from Bon Secours Hospital, Dublin. Costs of the treatments are calculated assuming patient body weight of 60 kg and body surface area of 1.75 $m^2$. The cost of palliative care was calculated by dividing the total spent on palliative care in 2011, €81 000 000, by the total number who availed of palliative care, 6000, giving an estimate of €13 500 [15,16]. Since there is no agreed upon costing method used in Irish economic evaluations, we adopt the strategy of the Guidelines for the Economic Evaluations of Health Technologies in Ireland and vary the costs between ± 20% of their mean value.

## Results

*Disease free survival analysis*

The costs, effects and transition probabilities were all entered into the model. In Figure 2, the calibration curves show that the model accurately represents five-year patient survival. The first panel of Table II shows the relapses per patient for this five-year period and the number needed to treat (NNT) to prevent one relapse. The increase in DFS for the five hazard ratios (0.9, 0.8, 0.7, 0.6, and 0.5) ranges from two to nine percentage points and the NNT ranges from 50 patients to 11 patients. DFS is inversely related to the NNT and so the NNT decreases as DFS increases. The total cost of preventing one relapse (NNT X cost of lapatinib) falls as the hazard ratio decreases and we can expect adjuvant lapatinib to become more cost-effective as the hazard ratio decreases, the NNT decreases and DFS increases.

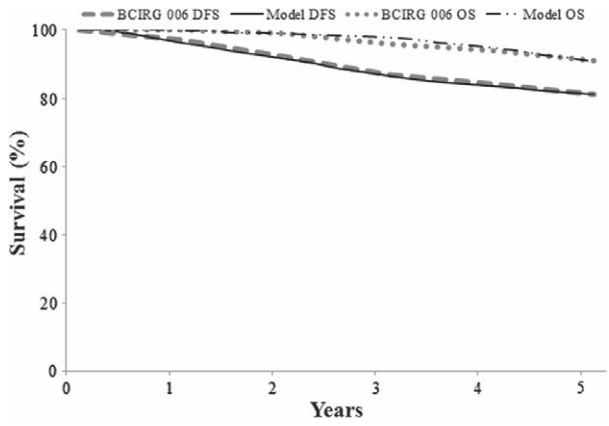


Figure 2. Markov model calibration curves. BCIRG 006 DFS, disease free survival curve from the BCIRG 006 trial [2]; BCIRG 006 OS, overall survival curve from the BCIRG 006 trial [2]; Model DFS, disease free survival curve from the Markov model; Model OS, overall survival curve from the Markov model.

*Base case analysis*

The base case analysis of the lifetime model is presented in the middle panel of Table II. In the Irish setting, even though there is no explicit threshold for cost-effectiveness, new treatments which have an ICER that is below €45 000/QALY tend to be reimbursed. The ICERs for the five hazard ratios are €53 089/QALY, €27 893/QALY, €18 463/QALY, €13 527/QALY and €10 490/QALY, respectively. Using the €45 000/QALY threshold, an adjuvant lapatinib regimen is cost-effective at the 0.8 hazard ratio where the ICER is €27 893/QALY. Using the TreeAge software we can pinpoint the exact hazard ratio when the treatment crosses the cost-effectiveness threshold, which is at 0.879, where the ICER is €44 825/QALY.

*Probabilistic sensitivity analysis*

In order to take account of uncertainty, we performed PSA on the model by using second order Monte Carlo simulations (1000 simulations) where values for probabilities, utilities and costs are allowed to be varied within a distribution. The results from this are also presented in Table II. The ICERs derived from the PSA are broadly similar to the ones calculated in the base case analysis. In addition, we were able to construct 95% confidence intervals through

Table II. Disease free survival, base case and probabilistic sensitivity analysis.

| | Disease free survival analysis | | | |
|---|---|---|---|---|
| Strategy | Relapses per patient | Inc. Relapses | NNT | Total cost of preventing one relapse |
| TCH | 0.19 | – | – | – |
| TCH + Lapatinib (HR = 0.9) | 0.17 | −0.02 | 50 | €496 692 |
| TCH + Lapatinib (HR = 0.8) | 0.16 | −0.03 | 33 | €327 817 |
| TCH + Lapatinib (HR = 0.7) | 0.14 | −0.05 | 20 | €198 677 |
| TCH + Lapatinib (HR = 0.6) | 0.12 | −0.07 | 14 | €139 074 |
| TCH + Lapatinib (HR = 0.5) | 0.10 | −0.09 | 11 | €109 272 |

| | Base case analysis | | | | |
|---|---|---|---|---|---|
| Strategy | Cost | QALY | Inc. Cost | Inc. QALY | ICER |
| TCH | €64 778.42 | 11.65 | – | – | – |
| TCH + Lapatinib (HR = 0.9) | €74 634.08 | 11.83 | €9855.66 | 0.19 | €53 089.00/QALY |
| TCH + Lapatinib (HR = 0.8) | €74 371.58 | 11.99 | €9593.16 | 0.34 | €27 892.76/QALY |
| TCH + Lapatinib (HR = 0.7) | €74 102.97 | 12.15 | €9324.55 | 0.51 | €18 463.36/QALY |
| TCH + Lapatinib (HR = 0.6) | €73 828.15 | 12.32 | €9049.73 | 0.67 | €13 527.38/QALY |
| TCH + Lapatinib (HR = 0.5) | €73 547.00 | 12.48 | €8768.58 | 0.84 | €10 490.38/QALY |

| | Probabilistic sensitivity analysis | |
|---|---|---|
| Strategy | ICER | 95% confidence interval |
| TCH + Lapatinib (HR = 0.9) | €55 296/QALY | €52 371/QALY–€58 475/QALY |
| TCH + Lapatinib (HR = 0.8) | €28 396/QALY | €27 423/QALY–€29 349/QALY |
| TCH + Lapatinib (HR = 0.7) | €18 637/QALY | €18 132/QALY–€19 110/QALY |
| TCH + Lapatinib (HR = 0.6) | €13 599/QALY | €13 275/QALY–€13 927/QALY |
| TCH + Lapatinib (HR = 0.5) | €10 515/QALY | €10 272/QALY–€10 763/QALY |

HR, hazard ratio; ICER, incremental cost-effectiveness ratio; Inc., incremental; NNT, number needed to treat; QALY, quality-adjusted life-year; TCH, regimen of docetaxel, carboplatin and trastuzumab.

bootstrapping (1000 replications). At a hazard ratio of 0.8, adjuvant lapatinib has an ICER of €28 396/QALY [95% confidence interval (CI) €27 423/QALY–€29 349/QALY]. We were able to use these estimates to calculate cost-effectiveness acceptability curves which are displayed in Figure 3. At a hazard ratio of 0.8, adjuvant lapatinib has a 100% probability of being cost-effective.

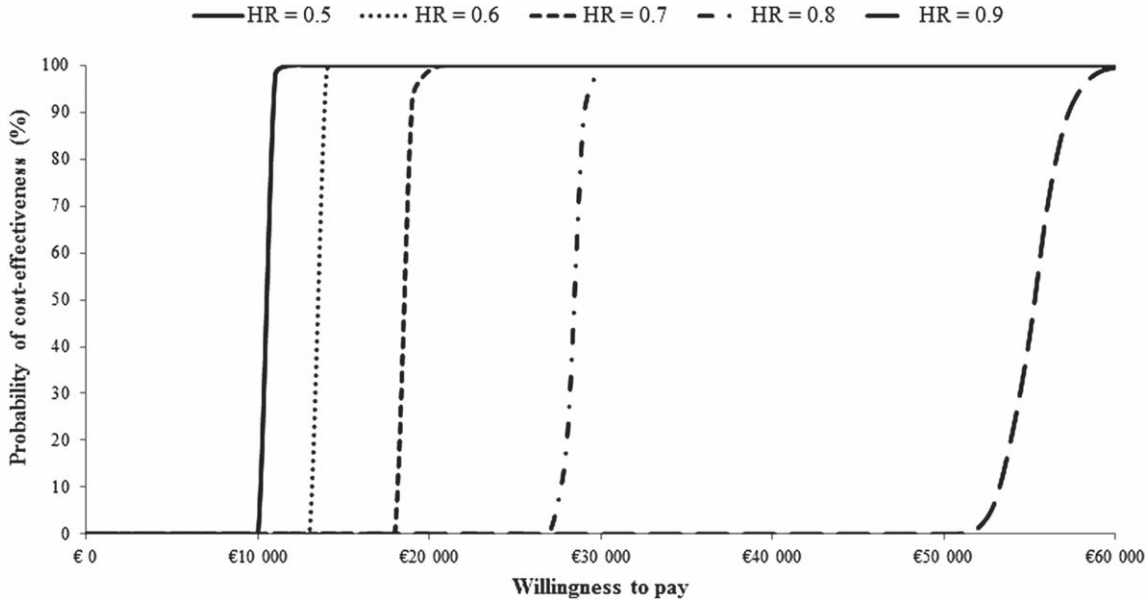


Figure 3. Cost-effectiveness acceptability curves. HR, hazard ratio.

*One-way sensitivity analysis*

We also conducted a number of one-way sensitivity analyses to examine the effect that individual parameters had on the model. The parameters we chose to vary were the price of lapatinib, the discount rate, limiting the length of the model, length of lapatinib efficacy, health state utilities, the cost of relapse treatment and the cost of palliative care. Since it would be cumbersome and excessive to perform this amount of analysis on five different hazard ratios we have chosen one hazard ratio to do one-way sensitivity analysis.

The hazard ratio we run the sensitivity analysis on is 0.83 because of the results of the TEACH trial [17]. The TEACH trial, in which patients with HER2-positive disease were randomly assigned to receive lapatinib or placebo following completion of conventional non-trastuzumab containing adjuvant chemotherapy produced a non-statistically significant hazard ratio of 0.83 (95% CI 0.7–1.0) for the use of lapatinib in the adjuvant setting. The base case ICER for the 0.83 hazard ratio is €32 661/QALY.

In Figure 4, the tornado diagram shows the effects that the individual variables have on the results. The variables which have the largest effect on the ICERs are the duration of efficacy of lapatinib, the discount rate, the length of the model and the costs of lapatinib. The health state utilities, cost of relapse treatment and cost of palliative care have a negligible effect on the ICERs. In all cases adjuvant lapatinib remains below the €45 000/QALY threshold.

## Conclusion

Lapatinib has an established role in the treatment of metastatic breast cancer, and is currently undergoing intense evaluation in the treatment of earlier stage disease, in both the pre-operative and post-operative adjuvant phases [3,18,19]. Taken collectively, the results of the NeoALTTO, NSABP B-41 and the EGF104900 study in metastatic disease, tend to support the hypothesis that combined HER2 antagonism may be superior to single antagonists [20,21]. We developed a model to test the potential cost-effectiveness of such combined inhibitor treatment based on a series of hypothetical assumptions of the relative hazard ratio for such treatment versus single inhibitors. Our model finds adjuvant lapatinib plus trastuzumab to be cost-effective for four of the five hazard ratios.

In the next few years, the results of the actual efficacy of lapatinib in treating early-stage breast cancer will become available. However, it is important for the oncology community to be aware, now, of the potential benefits that an adjuvant lapatinib regimen may have in terms of the QALYs gained by patients and whether these gains are cost-effective. This study attempts to provide answers to both questions. Finally, our study suggests that lapatinib could be more cost-effective in the treatment of earlier stage disease than it is in the treatment of metastatic cancer, where several jurisdictions have declined to approve it [22,23].

In these cases, the ICERs were well above the societal willingness to pay thresholds, possibly due to the high cost or low efficacy of the drug. However, by using lapatinib to treat early-stage breast cancer, these ICERs may be reduced with decreases in the drug's cost and increases in its efficacy. These decreases may occur by having to use less of the drug in adjuvant treatment compared to metastatic treatment and savings due to relapses prevented. Increases in efficacy could arise through a number of different mechanisms such as treating the cancer before it metastasises, complementarity from using it in

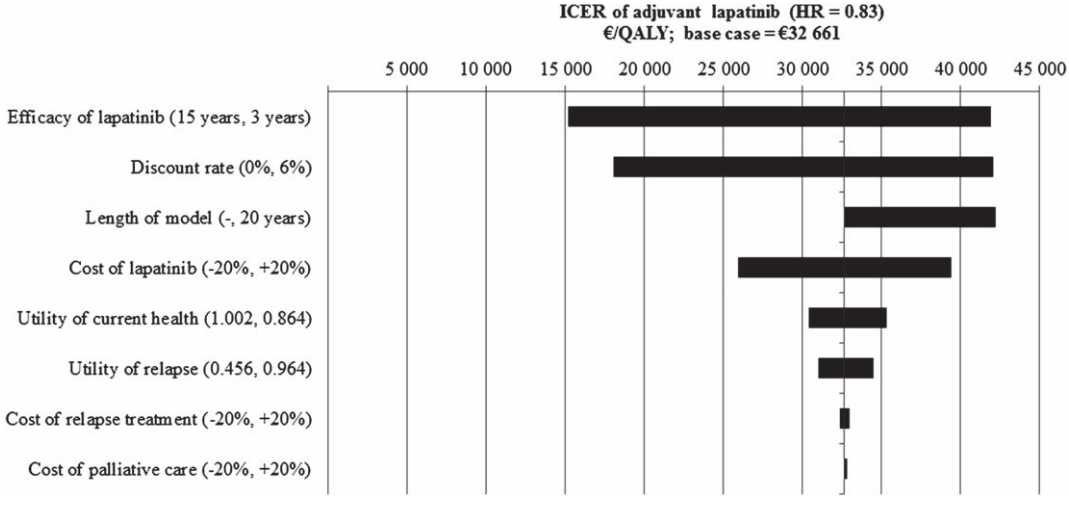


Figure 4. Tornado diagram. HR, hazard ratio; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

conjunction with trastuzumab, and patients enjoying longer life from being treated earlier. These hypotheses are supported by the results, but confirmation will require survival data from NeoALTTO and other studies.

The results of the NeoALTTO and TEACH trials suggest a cost-effective hazard ratio in favour of combined HER2 antagonism is plausible. The pCR rates from the NeoALTTO trial (51.3%, 29.5% and 24.7%) showed a combination of lapatinib and trastuzumab to be far superior to either antagonist alone and, in HER2 patients, response rates can be a powerful surrogate marker of survival rates [3]. In the NOAH trial, neoadjuvant and adjuvant trastuzumab plus neoadjuvant chemotherapy resulted in 43% level of pCR compared to only 22% in the neoadjuvant chemotherapy alone arm. Event free survival was also higher in the trastuzumab arm (hazard ratio = 0.58) after three years. By examining pCR rates and survival in the one study we can directly see the effect that pCR rates have on subsequent survival [4]. Based on these examples we are confident the hazard ratio for adjuvant lapatinib is $< 1$ and our analysis examines its cost-effectiveness across a wide spectrum of possible outcomes.

In the TEACH trial, patients with HER2-positive disease were randomly assigned to receive lapatinib or placebo following completion of conventional non-trastuzumab containing adjuvant chemotherapy. This likely suboptimal lapatinib schedule produced a non-statistically significant hazard ratio of 0.83 (95% CI 0.7–1.0) for the use of lapatinib in the adjuvant setting [17]. Considering that we predict that a hazard ration of only 0.879 would be required for adjuvant lapatinib to be considered cost-effective, an effect size of this magnitude would suffice. The ICER at this hazard ratio, €32 661/QALY, was also insensitive to a number of parameters in the sensitivity analysis.

We are confident that our analysis is accurate for a number of reasons. The first is the extensiveness of our sensitivity analysis, which shows that adjuvant lapatinib is cost-effective under a multitude of scenarios. The second reason is the accuracy of the cost data, most of which is taken from St. Vincent's Private Hospital in Dublin. Finally, this study is conducted in accordance with the National Centre for Pharmacoeconomics (NCPE) guidelines on cost-effectiveness analysis. These guidelines are based on the NICE guidelines in the UK and, therefore, our methods are widely generalisable to other health systems which use similar assessment techniques such as the UK, Canada and Australia.

There are limitations to this study. The BCIRG 006 study does not provide information on the type of patient recurrences so we do not differentiate between local/regional recurrences and distant recurrences. Therefore all relapses are treated as distant recurrences. While it is possible that including local/regional recurrences may increase the ICERs, the one-way sensitivity analysis showed that a 20% increase in relapse treatment costs had a negligible effect on the ICERs. If local/regional recurrences can be thought of as an extension of metastatic treatment this shows that not including them has no effect on the results. We do not include any information on testing costs for HER2. Since we compare two treatments for HER2 patients, we assume that testing would already be carried out prior to treatment. Even though we have tested the cost-effectiveness of a potential adjuvant lapatinib regimen, we have not assessed the full economic impact that using this treatment would have on the healthcare provider. With trastuzumab already costing €40 000, health systems do not have the resources to continually fund new additional therapies, which cost the same amount, ad infinitum. The addition of an 18-week course of lapatinib though, is less than €10 000. With the average incidence of early-stage breast cancer in Ireland being 2200 (2700 for all breast cancer) cases per year, 440 (20%) would be HER2 patients. This means it would cost the Irish health system an additional €4 400 000 to treat the entire number of new cases while saving somewhere between 84 and 370 QALYs. However, we refrain from conducting a full budget impact analysis until an adjuvant lapatinib regimen is commissioned for use.

In conclusion, an adjuvant lapatinib regimen would be considered cost-effective for patients with HER2-positive early-stage breast cancer for four of the five hypothesised hazard ratios. Data from both adjuvant and neoadjuvant trials suggest that the hazard ratio required to achieve cost-effectiveness for adjuvant lapatinib is both possible and plausible.

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