# Cost-Effectiveness Analysis of Sequential Paclitaxel Adjuvant Chemotherapy for Patients with Node Positive Primary Breast Cancer

Supon Limwattananon MPHM, PhD*, Chulaporn Limwattananon MPharm, MSc, PhD*, Savitree Maoleekulpairoj MD**, Noppadol Soparatanapaisal MD***

** Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen*
*** Medical Record Auditing Project, Health Systems Research Institute*
**** Faculty of Medicine, Siriraj Hospital, Mahidol University*

*An economic evaluation of paclitaxel added subsequently to doxorubicin plus cyclophosphamide (AC) adjuvant therapy for early breast cancer with lymph nodes positive is presented. Health care cost associated with AC alone vs. AC with paclitaxel was compared under Thai health care context. Based on CALGB9344, paclitaxel increased the disease-free survival (DFS) by 17%. Based on Markov simulation for 15 years, paclitaxel prolonged the patient's life by 0.30 quality-adjusted life years (QALY). Such an increased effectiveness was off set by the adjuvant cost net of recurrence, follow-up, and terminal care by 221,433 Baht. This means an additional year of perfect health gained by paclitaxel is achieved through an incremental cost of 738,111 Baht. Such an incremental cost-effectiveness ratio (ICER) is beyond the threshold recommended by World Health Organization. In women with negative estrogen receptor that DFS was improved to 28%, the ICER of paclitaxel was reduced to 393,984 Baht per QALY.*

***Keywords:*** *Cost-effectiveness, Markov model, Adjuvant chemotherapy, Early-stage breast cancer, Taxanes, Paclitaxel*

***J Med Assoc Thai 2006; 89 (5): 690-8***
***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

In Thailand, breast cancer is the second most prevalent solid tumor in the female population with an estimated incidence rate of 17.2 per 100,000[1]. The total number of cases is expected to increase, thus making breast cancer the most prevalence instead of cervical cancer[2]. Use of an adjuvant systemic chemotherapy for early-stage breast cancer (EBC) has been proven to improve disease-free and patient survivals[3,4]. The National Cancer Institute of Thailand has recommended (1) cyclophosphamide, methotrexate, and fluorouracil (CMF); (2) doxorubicin and cyclophosphamide (AC); (3) cyclophosphamide, doxorubicin and fluorouracil (CAF); and (4) cyclophosphamide, epirubicin and fluorouracil (CEF) as the standard adjuvant chemotherapy for EBC[5]. Previous randomized controlled trials (RCT) have demonstrated increasing clinical benefits of adding paclitaxel or docetaxel to the anthracycline-based regimens[6-9]. However, taxanes-containing chemotherapy is recommended by the national guideline only for selected patients with a high risk of relapse[5]. In the current National List of Essential Medicines, paclitaxel is restricted for patients who have not responded to anthracyclines in metastatic disease[10].

To date, economic evaluation of chemotherapy for EBC is limited. The present study is the first economic evaluation of the adjuvant chemotherapy in Thailand. The present study aims to determine whether the use of sequential paclitaxel is a cost-effective alternative in the adjuvant setting under the Thai health care context.

*Correspondence to : Limwattananon S, Department of Social and Administrative Pharmacy, Faculty of Pharmaceutical Sciences, Khon Kaen University, Amphoe Muang, Khon Kaen, 40002, Thailand. Phone: 0-4336-2090, Fax: 0-43202-379, E-mail: supon@kku.ac.th*

## Material and Method

The intervention of interest was the use of paclitaxel (175 mg/m$^2$ IV) for 4 cycles following a completion of 4 cycles of anthracycline-based regimen, which included doxorubicin (60 mg/m$^2$ IV) plus cyclophosphamide (600 mg/m$^2$ IV) or AC. The authors' target population was premenopausal EBC women who had axillary lymph nodes positive. Economic value of adding paclitaxel to AC was reflected by difference between the two interventions in total costs, compared with the outcome difference according to an incremental cost-effectiveness ratio (ICER) below.

$$\text{ICER} = \frac{\text{Total cost}_{\text{with paclitaxel}} - \text{Total cost}_{\text{without paclitaxel}}}{\text{Effectiveness}_{\text{with paclitaxel}} - \text{Effectiveness}_{\text{without paclitaxel}}}$$

The authors estimated long-term cost and effectiveness associated with the two treatment interventions over 15-year period using a mathematical simulation called Markov model[11-13]. Through the defined time horizon, the model simulated courses of relapse and progression of the disease repeatedly for a hypothetical cohort of EBC. In a yearly cycle, each cohort entered one of the following health states: no disease, localized disease, metastatic disease, and death (Fig. 1).

Probabilities of health state transition were derived from estimated risks of relapse and progression of the disease. For each cycle, fractions of the cohort were allocated to each health state according to the transitional probabilities.

The perspective taken for the authors' analysis belonged to the third-party payer such as health insurance scheme. As such, only direct health care cost was accounted for in the analysis. Cost associated with health care resource use in each treatment arm could be classified into two groups: initial cost (i.e., cost of adjuvant medication) vs. downstream cost (i.e., treatment for adverse drug events, routine follow up care, treatment for the disease recurrence, and care at the end of the patient's life). Based on a bottom-up approach, the total costs were decomposed into quantification and valuation of the resource usage into monetary terms. Patterns of the resource usage were based on the Thai health care context and the monetary values of unit prices were as of the year 2004.

As a measure of treatment outcomes, long-term effectiveness was enumerated in two terms: life years (LY) and quality-adjusted life years (QALY). Patient's life expectancy was estimated by aggregating the expected times spent in each health state over the 15-year horizon. Oncology patients rarely had a full

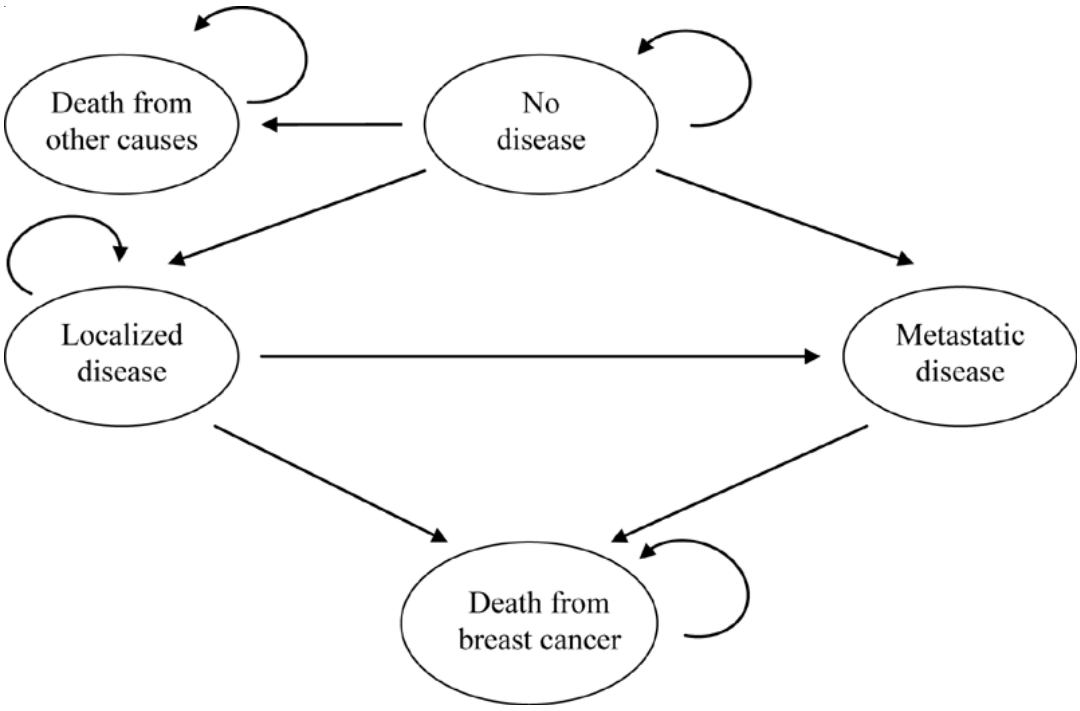


**Fig. 1** Health state transition in cohorts of early-stage breast cancer

quality of life during their surviving years. Therefore, QALY was an appropriate measure of the long-term outcome, which accounted for the preference placed on health states. This qualitative measure was represented by utility scores, ranging from the minimum of 0 (death) to the maximum of 1 (perfect health).

Information on clinical efficacy in terms of the disease-free survival, overall survival and quality of life for health states were derived from randomized controlled clinical trials (RCT) and published oncology literature. In the reference case, both cost and quality of life occurring from the second year cycle were discounted to the present values using the rate of 3% per year as recommended by an international guideline[14]. The non-discounted and 5%-discounted future cost and quality of life were submitted to a sensitivity analysis. The authors used DATA 3.5[15], a decision analysis computer software to run model simulation of the patient cohort.

***Health state transition***

Risk of an initial relapse for AC alone arm was based on an RCT by Cancer and Leukemia Group B (CALGB9344)[6] which reported the rates of disease-free survival (DFS) in the control group as 92, 81, 70, 65, and 58% at years 1, 2, 4, 5, and 7, respectively. The authors imputed the risks for years 8-15 using a linear trend extrapolation. The annual risks of initial relapse for paclitaxel arm were based on point estimate of hazard ratio (HR) of 0.83 obtained from the same RCT. The ratio of 1:9 was assumed to both treatment arms for partitioning the total relapse into localized and metastatic diseases. To account for the best clinical efficacy of paclitaxel reported in patient subgroup with negative estrogen receptor, the HR of 0.72 was used in a sensitivity analysis. Moreover, the upper limit of 95% confidence interval of the referent HR (i.e., 0.94) was used to reflect the worst case scenario.

The transitional probabilities of disease progression from localized and metastatic states were unlikely to vary across the treatment arms. Annual risks of death upon the two disease states were assumed to decline gradually over time. Data on the progression from localized disease to metastatic disease and to death, and from the metastatic disease to death were obtained from a published literature, which reported the probabilities at year 6 onward of 0.38, 0.08, and 0.22, respectively[16].

***Quality of patient's life***

Utility scores were derived from a survey of oncology nurses that was reported in a previous study[16]. Independent of the chemotherapy given, the utilities of 0, 0.62, 0.65, and 0.85 were assigned to death, metastatic disease, localized disease, and 'no disease' states, respectively. Based on the reported utility of 0.72 for chemotherapy use, the utilities for 3-month use of AC alone and 6-month use of paclitaxel following AC would be equal to 0.8175 and 0.785, respectively.

***Health care cost***

Valuation of chemotherapy medication was based on drug acquisition cost appearing in the manufacturers' price lists (Table 1). Notably, the acquisition cost for paclitaxel used in the reference case was for branded Taxol 100-mg vial. To accommodate variation in the unit costs across different versions of paclitaxel products, a 40% reduced price was submitted to further sensitivity analysis. Unit prices for other medication were available upon request to the authors.

To reflect the perspective of health care payers, all drug acquisition costs were marked up by 30% to reflect the charges hospitals typically made to payers. By multiplying the unit prices with amount of drug use, total costs of chemotherapy for a course of

**Table 1.** Acquisition costs for chemotherapy

| Generic name | Brand name and strength per package | Cost per package |
|---|---|---|
| Doxorubicin IV | Adriblastina 50 mg vial | 4,900 Baht |
| Cyclophosphamide IV | Endoxan 500 mg vial | 180 Baht |
| Paclitaxel IV | Taxol 100 mg vial | 15,320 Baht |
| Capecitabine PO | Xeloda 500 mg tablet | 158 Baht |
| Vinorelbine IV | Navelbine 50 mg vial | 11,689 Baht |
| Gemcitabine IV | Gemzar 200 mg vial | 2,171 Baht |

Source: Drug manufacturers' price lists (various sources)

**Table 2.** Amount of use of chemotherapy and associated costs

| Drug | Dose | Frequency | Total amount[a] | Cost[b] |
|---|---|---|---|---|
| Adjuvant medication | | | | |
| Doxorubicin IV | 60 mg/m$^2$ | 4 cycles | 384 mg | 48,922 Baht |
| Cyclophosphamide IV | 600 mg/m$^2$ | 4 cycles | 3,840 mg | 1,797 Baht |
| Paclitaxel IV | 175 mg/m$^2$ | 4 cycles | 1,120 mg | 223,059 Baht |
| Recurrence treatment | | | | |
| Paclitaxel IV | 175 mg/m$^2$ | 6 cycles | 1,680 mg | 334,589 Baht |
| Capecitabine PO | 2,500 mg/m$^2$ | 14 days x 4 cycles | 224,000 mg | 92,019 Baht |
| Capecitabine PO | 2,500 mg/m$^2$ | 14 days x 8 cycles | 448,000 mg | 184,038 Baht |
| Vinorelbine IV | 30 mg/m$^2$ | 2 days x 4 cycles | 384 mg | 116,703 Baht |
| Gemcitabine IV | 1,000 mg/m$^2$ | 2 days x 4 cycles | 12,800 mg | 180,627 Baht |

[a] based on the average body surface area of 1.6 m$^2$
[b] included the 30% mark up of acquisition cost

adjuvant and recurrence treatments are presented in Table 2.

Adding the operating costs for concomitant medication and medical supplies, IV administration, and outpatient service, the initial costs of adjuvant therapy were 277,531 and 52,595 Baht in total for AC with paclitaxel arm and for AC alone arm, respectively.

For an estimation of the downstream cost due to recurrence treatment, chemotherapy regimens were elicited through the opinions from a panel of oncology experts. Throughout the surviving period, the patient with disease recurrence who should receive three more regimens of chemotherapy could incur the cost of up to 549,878 Baht (due to the use of paclitaxel, capecitabine, and vinorelbine) for AC alone arm in all years. For recurrence in paclitaxel arm, use of capecitabine, vinorelbine, and gemcitabine would cost 487,936 Baht. To account for partial adherence to the recurrence treatment, cost of the first single regimen was submitted to further sensitivity analysis.

Even though use of a single paclitaxel is less likely to cause febrile neutropenia, the authors abstracted the adverse event probabilities from BCIRG 001 study for the reference case analysis. The incidence of febrile neutropenia was reported 24.7% for the taxane-based TAC and 2.5% for the anthracycline-based FAC[8]. The authors calculated the treatment cost per an event of febrile neutropenia at 14,406 Baht (details upon request). To bias in favor of paclitaxel for the sensitivity analysis, the adverse incidences between paclitaxel and no paclitaxel was assumed to be indifferent or zero.

The last episodic downstream cost was incurred by care at the terminal stage of cancer. The 6-month cost of medication plus 1.5 courses of palliative radiation therapy was estimated at 32,544 Baht (details upon request). A double and half of the reference case's terminal care cost were used for sen-sitivity analysis.

Downstream costs due to the routine follow up care for the states of no disease and localized and metastatic diseases were calculated based on recommendations made by national guideline in Thailand[5] which was adapted from the American guideline[17]. Resource use included physical examination (twice a year in the first three years and once a year thereafter) and mammography (once a year). The annualized cost was estimated as 2,800 Baht for years 1-3 and 2,300 Baht for years 4-15.

## Results

Proportions of patient cohorts entering each of the four health states in a given year are presented in Table 3. Over the 15-year time horizon, total durations a patient spent in the states of no disease, localized disease, and metastatic disease were 9.00, 0.08, and 1.53 years for paclitaxel and 8.32, 0.09, and 1.73 years for AC alone, respectively. In sum, the patients receiving paclitaxel lived in the no disease state 0.68 years longer and spent 0.21 years in the disease recurrence states shorter than those receiving AC alone.

The result showed the overall survival rates at the end of the study period of 54.0% for paclitaxel arm and 38.5% for AC alone arm (Fig. 2). Compared with the last year data in CALGB, proportions of the patients remaining alive after year 7 in our simulating model (73.7% for paclitaxel and 69.8% for AC alone) are close to that reported by the referent paper (74 and 68% for paclitaxel and AC alone, respectively).

**Table 3.** Proportion of cohorts entering health states by years

| Year | No Paclitaxel | | | | With Paclitaxel | | | |
|---|---|---|---|---|---|---|---|---|
| | Death | Metastatic disease | Localized disease | No disease | Death | Metastatic disease | Localized disease | No disease |
| 1 | 0.5% | 7.1% | 0.8% | 91.6% | 0.5% | 5.9% | 0.7% | 92.9% |
| 2 | 5.0% | 10.3% | 0.8% | 83.9% | 4.3% | 8.7% | 0.7% | 86.3% |
| 3 | 10.1% | 15.4% | 1.1% | 73.4% | 8.7% | 13.1% | 0.9% | 77.2% |
| 4 | 15.7% | 15.4% | 0.8% | 68.1% | 13.5% | 13.3% | 0.7% | 72.5% |
| 5 | 21.2% | 15.3% | 0.7% | 62.7% | 18.4% | 13.2% | 0.7% | 67.7% |
| 6 | 26.7% | 14.7% | 0.7% | 58.0% | 23.1% | 12.8% | 0.6% | 63.4% |
| 7 | 30.2% | 14.5% | 0.7% | 54.6% | 26.3% | 12.8% | 0.6% | 60.3% |
| 8 | 33.8% | 14.3% | 0.7% | 51.2% | 29.5% | 12.8% | 0.6% | 57.1% |
| 9 | 37.2% | 13.9% | 0.6% | 48.3% | 32.6% | 12.4% | 0.6% | 54.4% |
| 10 | 40.6% | 13.1% | 0.6% | 45.8% | 35.7% | 11.9% | 0.5% | 51.9% |
| 11 | 43.7% | 12.3% | 0.5% | 43.5% | 38.6% | 11.2% | 0.5% | 49.7% |
| 12 | 46.7% | 11.3% | 0.4% | 41.6% | 41.4% | 10.4% | 0.4% | 47.8% |
| 13 | 49.4% | 10.3% | 0.4% | 39.8% | 43.9% | 9.6% | 0.4% | 46.2% |
| 14 | 51.9% | 9.4% | 0.3% | 38.4% | 46.3% | 8.7% | 0.3% | 44.7% |
| 15 | 54.2% | 8.4% | 0.3% | 37.1% | 48.4% | 7.9% | 0.3% | 43.4% |

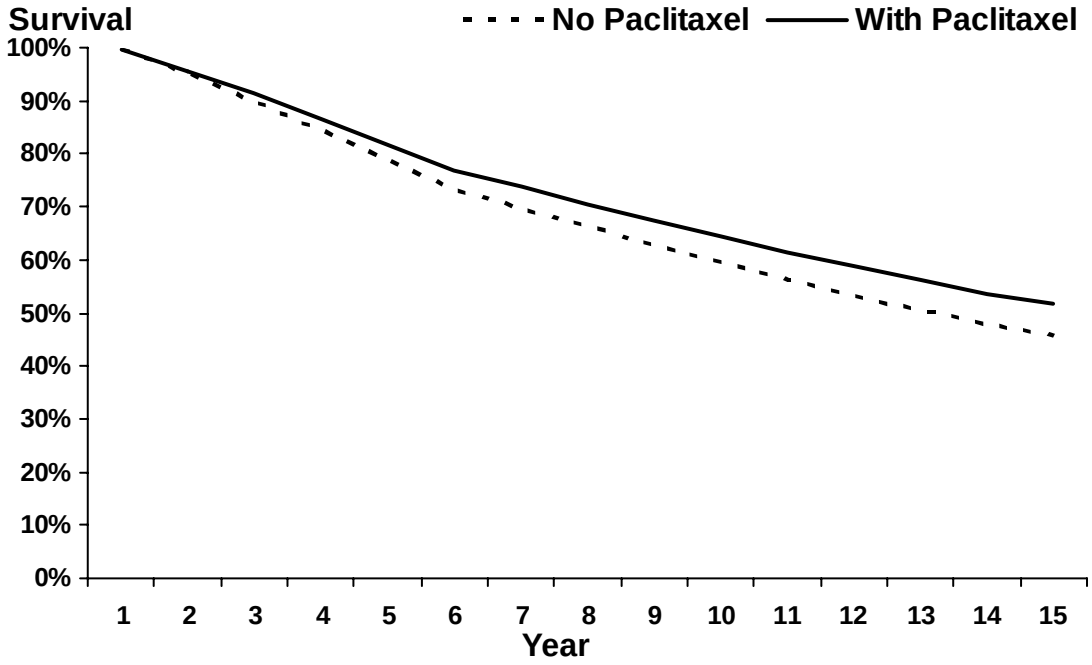


**Fig. 2** Overall survivals simulated by Markov model

For paclitaxel arm, the 15-year health care cost was estimated at 356,325 Baht in total. Almost 80% of the total cost was incurred by an administration of the adjuvant medication, mostly due to the expensive paclitaxel. Downstream use of health care resources associated with recurrence treatment, routine follow up, and terminal care was aggregated to 21% of the total cost. For AC alone arm, cost of the adjuvant administration contributed 39% to the total cost estimate (134,892 Baht). Combined cost of recurrence treatment,

follow up, and terminal care was the majority (61%). Despite paclitaxel being able to save the downstream cost over the AC use by 6,700 Baht, the initial cost introduced by an administration of paclitaxel was much higher (224,936 Baht).

An analysis of treatment effectiveness over 15 years of time horizon revealed that use of paclitaxel following AC and AC alone resulted in 10.61and 10.14 years of the patient's life expectancy, respectively. Taking into account the patient's quality of life, an addition of paclitaxel to AC generated 7.17 QALY, whereas 6.87 QALY were to the AC alone. This implies that paclitaxel could prolong the patient's life in terms of LY by 0.47 years, which was equivalent to 0.3 years with the full quality of life or QALY. However, such a clinical benefit gain came with an additional cost of 221,433 Baht to be paid for. In sum, use of paclitaxel as an adjuvant would incur the incremental cost of 738,111 Baht, on average, for each one of QALY gained.

Fig. 3 shows the results obtained from one-way sensitivity analysis using the possible range of key uncertain parameters in the simulation model.

The ICER of paclitaxel varied considerably with changes in the relative efficacy and unit price of paclitaxel. For the best-case scenario where paclitaxel the relative efficacy of paclitaxel was reduced to the HR of 0.94. A 40% reduction in the unit price of paclitaxel would lower the ICER to 446,823 Baht per QALY. The present study found that changes in the adverse event rates, treatment for recurrence, and cost of terminal care minimally affected the ICER sensitivity.

**Discussion**

In Western countries, previous studies found an increased effectiveness of the standard adjuvant CMF for EBC ranging from 1.09 to 3.57 years of life expectancy[18,19]. The additional health care costs per life year gained due to the treatment varied considerably from $447 to 2,973- 7,860. The present study revealed that use of paclitaxel following the standard AC regimen extended the patients' life by almost half year. Such an additional effectiveness implied cost saving due to the use of health care resources during disease recurrence and terminal stage at a modest value. Use of the adjuvant medication with paclitaxel would cost health care payers a lot more. Therefore, the additional clinical benefit of paclitaxel came with an increment of health care cost, which, on average, was equivalent to the ICER of 738,111 Baht per each QALY gained.

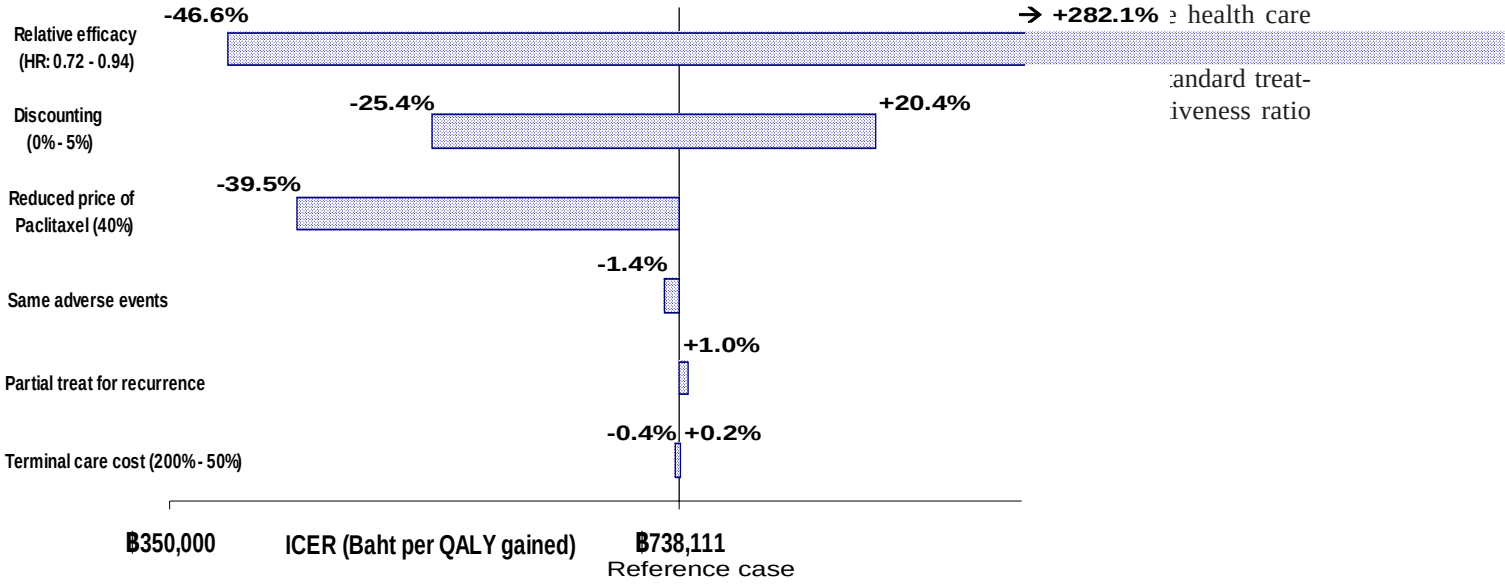


**Fig. 3** Sensitivity analysis results

(CER). Use of renal dialysis instead of palliative care incurred an additional cost per QALY gained of 615,980 and 667,643 Baht for continuous ambulatory peritoneal dialysis and for institutional hemodialysis, respectively[20]. For a developing country, World Health Organization (WHO) has recommended medical interventions of which CER below 3 times of per capita income to be deemed cost-effective[21]. In 2004, the gross national income per capita for Thailand was US$ 2,540 or 101,600 Baht per year[22]. Hence, an economic burden paclitaxel imposed on public schemes of health insurance lies far above the WHO-recommended cost-effectiveness criterion.

For paclitaxel to come close to cost-effective, the sensitivity analysis results revealed two influential parameters: relative clinical efficacy, and unit price of paclitaxel. In the patient subgroup with negative estrogen receptor, a 28% increase in DFS due to an addition of paclitaxel could bring down the ICER to 46.6% of the reference case. For the 40% reduced price of paclitaxel, the gap in adjuvant costs between the two competing arms would drop substantially to 135,712 Baht, which lowered the ICER by a comparable proportion (39.5%) to 446,823 Baht per QALY. However, such CER is still beyond the acceptable limit.

Major limitation of the present study came with an enumeration of the effectiveness. To the authors' knowledge, well-designed studies on paclitaxel are not available in Thailand. With a large sample size (N = 3,121) and long-term follow up (69 months) of the referent RCT[6], the authors believe the data obtained for the present study are reliable in reflecting the risks of disease relapse and the relative efficacy of paclitaxel. For an estimation of cost, the present study follows the internationally accepted guideline by using the bottom up approach. As such, information on the quantity of resource use was presented separately from unit prices.

## Conclusion

The present study indicates use of paclitaxel and AC regimen in the adjuvant setting for EBC save resource use for the recurrence treatment at a modest amount. An initiation of paclitaxel costs a substantial amount of money compared with the standard anthracycline-based chemotherapy. Based on the WHO criterion, the additional benefit of subsequent use of paclitaxel on quality-adjusted life expectancy in all patients with axillary lymph node metastasis is not cost-effective. In a high-risk subset of patients with estrogen receptor negative and axillary node metastasis, the adjuvant paclitaxel comes close to the cost-effectiveness threshold based on the author's sensitivity analysis.

## Acknowledgement

The authors wish to thank the Medical Record Auditing Project of Health Systems Research Institute for funding this research.

## References

1. Martin N, Cheirsilpa A. Breast. In: Sriplung H, Sontipong S, Martin N, editors. Cancer in Thailand. Vol. III (1995-1997). Bangkok: Bangkok Medical Publisher; 2003: 47-8.
2. Sriplung H. Projection of cancer problems. In: Sriplung H, Sontipong S, Martin N, editors. Cancer in Thailand. Vol. III (1995-1997). Bangkok: Bangkok Medical Publisher; 2003: 82-4.
3. Bonadonna G, Valagussa P, Moliterni A, Zambetti M, Brambilla C. Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer: the results of 20 years of follow-up. N Engl J Med 1995; 332: 901-6.
4. Early Breast Cancer Trialists' Collaborative Group. Polychemotherapy for early breast cancer: an overview of the randomized trials. Lancet 1998; 352: 930-42.
5. Cheirsilpa A, Chaiverawattana A, Jariyaradsak S, editors. Clinical practice guideline for breast cancer: investigation and management 2003-2004. National Cancer Prevention and Control Program Board, National Cancer Institute of Thailand. Bangkok: Agricultural Cooperative Federation of Thailand Publisher; 2003: 54-79.
6. Henderson IC, Berry DA, Demetri GD, Cirrincione CT, Goldstein LJ, Martino S, et al. Improved outcomes from adding sequential paclitaxel but not from escalating doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. J Clin Oncol 2003; 21: 976-83.
7. Mamounous EP, Bryant J, Lembersky BC, Fehrenbacher L, Sedlacek SM, Fisher B, et al. Paclitaxel after doxorubicin plus cyclophosphamide as adjuvant chemotherapy for node-positive breast cancer: results from NSABP B-28. J Clin Oncol 2005; 23: 3686-96.
8. Nabholtz JM, Pienkowski T, Mackey J, Pawlick M, Guastalla JP, Vogel C, et al. Phase III trial comparing TAC (docetaxel, doxorubicin, cyclophosphamide) with FAC (5-fluorouracil, doxorubicin,

cyclophosphamide) in the adjuvant treatment of node positive breast cancer patients: interim analysis of the BCIRG 001 study [abstract]. Proc Am Soc Clin Oncol 2002; 21: 141.
9. Martin M, Pienkowski T, Mackey J, Pawlicki M, Guastalla JP, Weaver C, et al. TAC improves disease free survival and overall survival over FAC in node positive early breast cancer patients, BCIRG 001: 55 months follow-up Breast Cancer Research and Treatment, 82: Special Issue: 26th Annual San Antonio Breast Cancer Symposium. 2003; abstract 43.
10. National Drug Committee. National List of Essential Medicines. Nonthaburi: Ministry of Public Health; 2004.
11. Beck JR, Pauker SG. The Markov process in medical prognosis. Med Decis Making 1983; 3: 419-58.
12. Naimark D, Krahn MD, Naglie G, Redelmeier DA, Detsky AS. Primer on medical decision analysis: part 5-working on the Markov process. Med Decis Making 1997; 17: 152-9
13. Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide. Med Decis Making 1993; 13: 322-38.
14. Gold MR, Siegel JE, Russell LB, Weinstein MC, editors. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.
15. DATA 3.5, Williamstown, MA: TreeAge Software Inc; 2001.
16. Lee JH, Glick HA, Hayman JA, Solin LJ. Decision-analytic model and cost-effectiveness evaluation of postmastectomy radiation therapy in high-risk premenopausal breast cancer patients. J Clin Oncol 2002; 20: 2713-25.
17. Smith TJ, Davidson NE, Schapira DV, Grunfeld E, Muss HB, Vogel VG III, et al. American Society of Clinical Oncology 1998 update of recommended breast cancer surveillance guidelines. J Clin Oncol 1999; 17: 1080-2.
18. Messori A, Becagli P, Trippoli S, Tendi E. Cost-effectiveness of adjuvant chemotherapy with cyclophosphamide + methotrexate + fluorouracil in patients with node-positive breast cancer. Eur J Clin Pharmacol 1996; 51:111-6.
19. Norum J. Adjuvant cyclophosphamide, methotrexate, fluorouracil (CMF) in breast cancer - is it cost-effective? Acta Oncol 2000; 39: 33-9.
20. Teerawattananon Y. Cost-effectiveness of renal replacement therapy in Thailand. In: Tangcharoensathien V, Kasemsap V, Supaporn T, Teerawattananon Y, editors. Universal access to renal replacement therapy in Thailand: a policy analysis. Nonthaburi: Health Systems Research Institute and National Health Security Office; 2005.
21. Commission on macroeconomics and health. Investing in health for economic development. Geneva: World Health Organization; 2001.
22. World Bank. World development indicators 2005. Washington, DC: World Bank; 2005.

## *การวิเคราะห์ต้นทุน-ประสิทธิผลของยา paclitaxel ในการรักษาเสริมมะเร็งเต้านมระยะเริ่มแรกที่มีการกระจายไปยังต่อมน้ำเหลือง*

**สุพล ลิมวัฒนานนท์, จุฬาภรณ์ ลิมวัฒนานนท์, สาวิตรี เมาฬีกุลไพโรจน์, นพดล โสภารัตนไพศาล**

*บทความนี้นำเสนอผลการประเมินทางเศรษฐศาสตร์สำหรับยา paclitaxel ซึ่งใช้ต่อจาก doxorubicin ร่วมกับ cyclophosphamide (AC) เพื่อการรักษาเสริมในมะเร็งเต้านมระยะแรก ต้นทุนทางสุขภาพจากการใช้ AC เปรียบเทียบกับ AC และ paclitaxel โดยใช้บริบทระบบสุขภาพของไทย จากการศึกษาของ CALGB-9344 พบว่าการเสริม paclitaxel สามารถเพิ่มอัตราการปลอดโรคได้ 17% จากการจำลองตัวแบบ Markov ในระยะเวลา 15 ปี พบว่า การใช้ paclitaxel สามารถยืดอายุผู้ป่วยได้ 0.30 ปีที่ปรับด้วยคุณภาพชีวิต (quality-adjusted life years, QALY) การเพิ่มขึ้นของประสิทธิผลดังกล่าวถูกชดเชยด้วยต้นทุนของการใช้ยารักษาเสริมเมื่อหักลบกับการรักษาการกลับเป็นซ้ำ การติดตาม และการดูแลผู้ป่วยระยะสุดท้ายเป็นเงินทั้งสิ้น 221,433 บาท หมายความว่าการเพิ่มขึ้น 1 ปีที่มีคุณภาพชีวิตสมบูรณ์จากการใช้ paclitaxel ได้จากการเสียค่าใช้จ่ายที่เพิ่มขึ้น 738,111 บาท อัตราส่วนของต้นทุน-ประสิทธิผล (ICER) ดังกล่าวมีค่ามากกว่าเกณฑ์ของความคุ้มค่าที่แนะนำโดยองค์การอนามัยโลก สำหรับในผู้หญิงที่ผลการตรวจชิ้นเนื้อ estrogen receptor ให้ผลลบซึ่ง paclitaxel เพิ่มอัตราการปลอดโรคได้ 28% ค่า ICER ของ paclitaxel ลดลงเป็น 393,984 บาทต่อ QALY*