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Cost-effectiveness of Tamoxifen versus Anastrozole in post-menopausal women with breast cancer: Saudi Arabia perspective

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ABSTRACT

Background: Tamoxifen and Anastrozole are widely used as adjuvant therapy for Hormone-sensitive early breast cancer patients. Although these medications are expensive, we lack cost-effectiveness analysis to inform decision-making.

Aim: We aim to assess the cost-effectiveness of Anastrozole versus Tamoxifen for the adjuvant therapy of hormone-positive tumors among postmenopausal women with early breast cancer.

Methods: A probabilistic Markov model was built considering The Arimidex, Tamoxifen, Alone, or in Combination (ATAC) trial outcomes for the model assumptions. The model is built from the Saudi perspective. Probabilistic sensitivity analysis was conducted for uncertainty.

Results: Anastrozole has been cost-effective with an incremental cost-effectiveness ratio of 80333.88 SAR/quality-adjusted life-year at a Willingness-to-pay of 100,000 USD (equivalent to 375,000 SAR). The probabilistic sensitivity analysis was conducted, and Anastrozole was still cost-effective under changing parameters.

Conclusion: Anastrozole offers a cost-effective adjuvant option for hormone-positive early breast cancer patients and can be considered for reimbursement.

Keywords: anastrozole; tamoxifen; breast cancer; cost-effectiveness analysis; incremental cost-effectiveness ratio (ICER)

INTRODUCTION

Breast cancer (BC) is the most prevalent cancer globally.[1] In 2020, 2.3 million females were diagnosed with breast cancer with 685, 000 deaths globally.[1] In Saudi Arabia (KSA), in 2020, the 5-year prevalence of BC was 92.99 per 100000,[2] making it the most common cancer in KSA.[3] The number of new cases was 13632 in 2020.[2] The estimated mortality due to BC is 8.4%.[2] Economically, treatment of breast cancer in KSA[4] costs approximately 13 million USD, with the average cost in a patient from 14,3 USD in stage I to 81 USD in stage IV. Hormone-receptor positive (HR+) tumors are the most common subtypes in KSA,[5] accounting for approximately 73% of the cases.

The traditional adjuvant treatment in HR+ tumors is Tamoxifen.[6] Unfortunately, it is related to serious safety concerns, such as thromboembolism. The aromatase inhibitor (Anastrozole) has shown lower thromboembolic adverse effects than Tamoxifen. Therefore, it is a valuable option for adjuvant treatment

of HR+ cases in postmenopausal patients.[6] Different studies have compared both medications as adjuvant hormonal treatments for early breast cancer (EBC) patients.[7,8]

Regarding spending on breast cancer in Saudi Arabia, medication cost consumes most of the budget.[4] Therefore, characterizing the economic evaluation of the commonly used medications is needed. The economic evaluation will help the decision-maker in reimbursement decisions to control the budget and offer the best available treatment for the patients.

Although these medications are commonly used in this patient population, there is no cost-effectiveness (CEA) study comparing them in Saudi Arabia. In our study, we identify the cost-effectiveness of both options.

MATERIALS AND METHODS

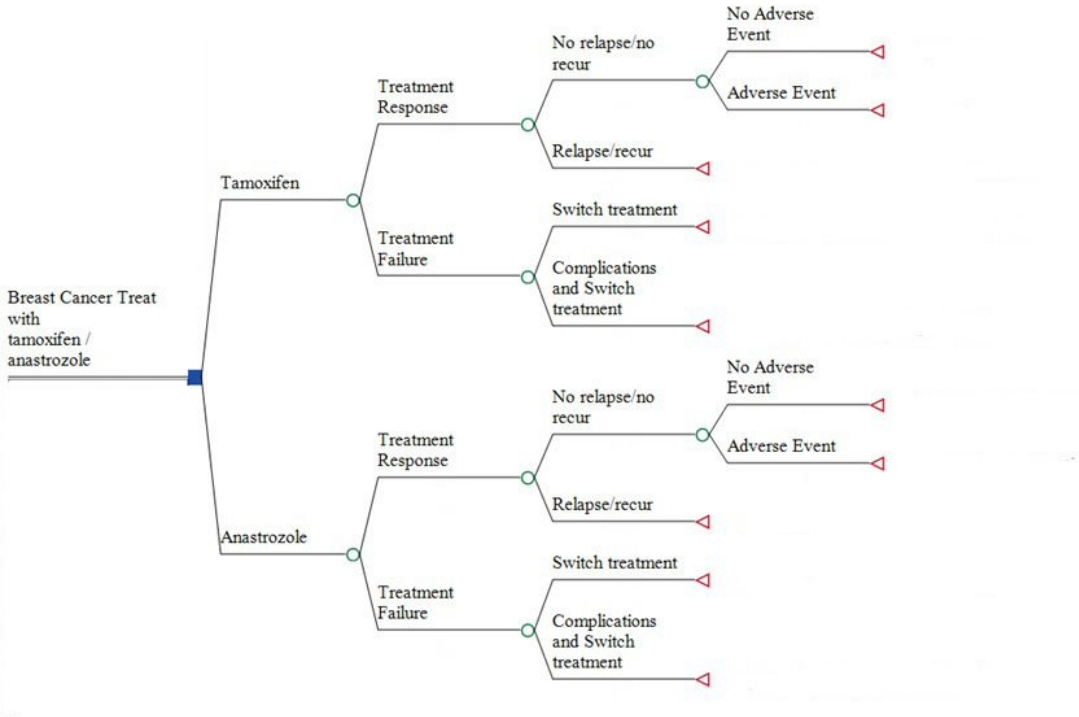
Study design

This study demonstrates an economic evaluation framework to compare the costs and effects of Tamoxifen 20 mg/day with Anastrozole 1 mg/day in postmenopausal females with early locally advanced HR+ breast cancer.

Model structure

A probabilistic Markov model was made to identify the outcomes for a group of 145 postmenopausal women (average age 57 years) suffering early BC in Saudi Arabia. The model was built using TreeAge Pro Suite 2008 (TreeAge Software Inc.). The model structure is presented in Figure 1. The model was built from the Payer perspective in Saudi Arabia, considering the direct medical cost.

Figure 1: Representation of the Markov model and decision tree showing transitions between states



A time horizon of 25 years was selected to recognize the effects of the treatment. An extended horizon would have added no more significant information about the outcomes, considering the mean age and the expected life duration of this patient population.

Patients move through seven states every three months during the primary five years and six months thereafter. These states are detailed below:

Patients on anastrozole or tamoxifen, patients switching adjuvant treatment without a prior plan, patients who are not on treatment, patients in remission with recurrence, patients with recurrence either regional or local, patients who died due to breast cancer, and patients who died due to any causes other than breast cancer. All women begin the model with either Tamoxifen or Anastrozole.

Major Assumption

It was assumed that the patients of The Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial[8] are representative of postmenopausal women with hormone-sensitive EBC in Saudi Arabia and the results apply to the Saudi population. The inclusion and exclusion of criteria of the patients are the same as in the ATAC trial.

Patient Population

The characteristics of the cohort are similar to the patients included in the Braal L. et al. study.[9] Patients included in the model are early postmenopausal, diagnosed with locally advanced estrogen-receptor-positive breast cancer with no contraindications for both comparators (Tamoxifen and Anastrozole). Women are considered in the menopause state if they fulfill one or more of the criteria of the National Comprehensive Cancer Network (NCCN)[10] definition of menopause.

Treatment Program

Patients in the model received either Anastrozole 1 mg/day or Tamoxifen 20 mg/day. Standard therapy was assumed to continue until the disease progresses. It was assumed that patients with marked breast cancer progression, dangerous side effects, noncompliance with procedures, or denial/inability to resume the trial were withdrawn. All patients who were withdrawn due to causes other than significant disease progression were followed every six months for survival.

Efficacy Assessments

The outcome measure used in the study is quality-adjusted life years (QALYs). Utilities for the different states were calculated using the standard gamble technique. The mean utility scores are briefed in table 1.

Probabilities

The model-attributed probabilities per group were derived from the ATAC trial, surmising a constant pattern along with the simulation. Beta distributions are commonly applied to model transition probabilities.[11]

Statistical Analysis

The ICER was calculated by subtracting the cost of Anastrozole from Tamoxifen and dividing the results by the outcome of the difference in QALYs applying a Monte Carlo simulation of 5000 iterations. Results are exhibited by mean values of costs and effects and as a cost-effectiveness acceptability curve (CEAC).

Sensitivity analyses

The distribution of the parameters affecting the outcome is presented in table 1. Probabilistic sensitivity analysis was run on these inputs with the CE plane shown in figure 1.

Cost estimation

The medication cost was obtained from the publicly available Saudi Food and Drug Authority (SFDA) Database

RESULTS

Considering QALY, the adjuvant therapy care with both Tamoxifen and Anastrozole yielded 0.84 discounted gained years; Neither strategy is dominant over the other. The outcomes of the model are shown in Table 2.

According to the mode, Anastrozole's incremental cost is +525 SAR (Saudi Arabian Riyal) than Tamoxifen. It has a higher incremental effect of 0.01 QALY. These results in ICER of 80,333.88 SAR/QALY. Which is below the assigned WTP of 100,000 USD (375,000 SAR).[12] The cost-effectiveness plane in figure 2 shows this result.

Table 1 | Outcome probabilities, costs of medical, and utility scores

	Probabilities	**Distribution**
Tamoxifen	0.555	Beta
Anastrozole	0.562	Beta
Tamoxifen, recurrences	0.5	Beta
Anastrozole, recurrences	0.5	Beta
Tamoxifen, adverse events	0.657	Beta
Anastrozole, adverse events	0.698	Beta
	Costs (USD)	
Tamoxifen	15	Gamma
Anastrozole	35	Gamma
	Utility	
Disease-free state, no AEs	0.965	Beta
AEs (tamoxifen)	0.959	Beta
AEs (anastrozole)	0.958	Beta
Local/regional recurrence	0.766	Beta
Current health	0.893	Beta

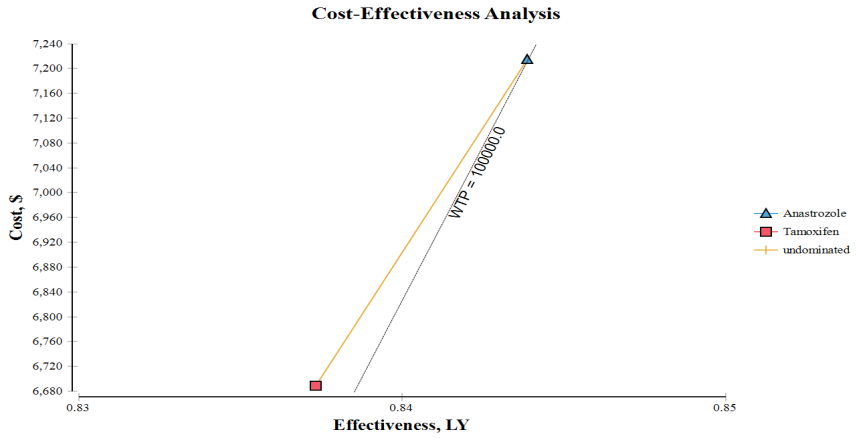
Abbreviations: USD: United States Dollars, AEs: adverse events

Table 2 | Base case results

Treatment Strategy	Cost	Incremental Cost	Effect	Incremental effect	(ICER)
Tamoxifen	6,689		0.84		
Anastrozole	7,214	525	0.84	0.01	80333.8

Abbreviations: C/E: cost-effectiveness, ICER: incremental cost-effectiveness ratio

Figure 2: Cost-effectiveness (CE) plane showing Anastrozole at the CE threshold



Sensitivity analyses

Sensitivity analyses were generated to examine the model uncertainties. However, Anastrozole remains a CE treatment form when varying parameters.

DISCUSSION

Anastrozole was compared to Tamoxifen as an adjuvant modality in postmenopausal females. The result was 0.01 QALYs attained in the group of females over a period of 25 years. Anastrozole was more cost-effective than Tamoxifen for this patient population when considering model inputs from the ATAC trial and under the assumptions given. The ICER was 80,333.88 SAR/QALY (equivalent to 21.422 USD/QALY), which is far less than the WTP assigned in the study, 100000 USD (equivalent to 375,000 SAR). According to the probabilistic sensitivity analysis, Anastrozole was still cost-effective even under all parameters changing. The results of our study come coherent with the results of earlier studies. Shih et al.[13] found that Anastrozole is cost-effective with ICER of S $114,061 /QALY gained.

Our study comes with some limitations. The carryover effect of Anastrozole was not considered during the analysis. This was done to simplify the model and the results. Also, the model didn't account for different changes in the mortality of the patients over the time horizon.

CONCLUSION

In conclusion, our study has shown Anastrozole is cost-effective in treating hormone-sensitive females with EBC. This result was consolidated in probabilistic sensitivity analysis and came in coherence with the models from different other countries.

Conflict of Interest

The author declares that there are no conflicts of interest relevant to this article.

REFERENCES

1. WHO. Breast cancer [Internet]. 2021 [cited 2022 May 24]. Available from: https://www.who.int/news-room/fact-sheets/detail/breast-cancer
2. International agency of research on cancer. Saudi Arabia Cancer Factsheet 2020 [Internet]. [cited 2022 May 24]. Available from: https://gco.iarc.fr/today/data/factsheets/populations/682-saudi-arabia-fact-sheets.pdf
3. Alqahtani WS, Almufareh NA, Domiaty DM, et al. Epidemiology of cancer in Saudi Arabia thru 2010-2019: a systematic review with constrained meta-analysis. *AIMS Public Health*. 2020;7(3):679-696.
4. Alghamdi A, Balkhi B, Alqahtani S, Almotairi H. The Economic Burden Associated with the Management of Different Stages of Breast Cancer: A Retrospective Cost of Illness Analysis in Saudi Arabia. *Healthcare (Basel)*. 2021;9(7):907.
5. Alnegheimish NA, Alshatwi RA, Alhefdhi RM, Arafah MM, AlRikabi AC, Husain S. Molecular subtypes of breast carcinoma in Saudi Arabia. A retrospective study. *Saudi Med J*. 2016;37(5):506-512.
6. Drăgănescu M, Carmocan C. Hormone Therapy in Breast Cancer. *Chirurgia (Bucur)*. 2017;112(4):413-417.
7. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Aromatase inhibitors versus tamoxifen in premenopausal women with oestrogen receptor-positive early-stage breast cancer treated with ovarian suppression: a patient-level meta-analysis of 7030 women from four randomised trials [published correction appears in Lancet Oncol. 2022 Apr;23(4):e161]. *Lancet Oncol*. 2022;23(3):382-392.
8. Cuzick J, Sestak I, Baum M, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. *Lancet Oncol*. 2010;11(12):1135-1141.
9. Braal CL, Kleijburg A, Jager A, et al. Therapeutic Drug Monitoring-Guided Adjuvant Tamoxifen Dosing in Patients with Early Breast Cancer: A Cost-Effectiveness Analysis from the Prospective TOTAM Trial. *Clin Drug Investig*. 2022;42(2):163-175.
10. National Comprehensive Cancer Network. Breast cancer guidelines Version 3.2022 [Internet]. NCCN.

[cited 2022 May 26]. Available from: https://www.nccn.org/guidelines/guidelines-detail

11. Briggs: Decision modelling for health economic evaluation - Google Scholar [Internet]. [cited 2022 May 24]. Available from: https://scholar.google.com/scholar_lookup?author=A+Briggs&author=M+Sculpher&author=K+Claxton+&publication_year=2006&title=Decision+Modelling+for+Health+Economic+Evaluation
12. Maraiki F, Bazarbashi S, Scuffham P, Tuffaha H. Methodological Approaches to Cost-Effectiveness Analysis in Saudi Arabia: What Can We Learn? A Systematic Review. *MDM Policy Pract*. 2022;7(1):23814683221086869. Published 2022 Mar 21.
13. Shih V, Chan A, Xie F, Ko Y. Economic Evaluation of Anastrozole Versus Tamoxifen for Early Stage Breast Cancer in Singapore. *Value Health Reg Issues*. 2012;1(1):46-53.