

Cost effectiveness of Cyclophosphamide in the adjuvant treatment of breast cancer in Spain

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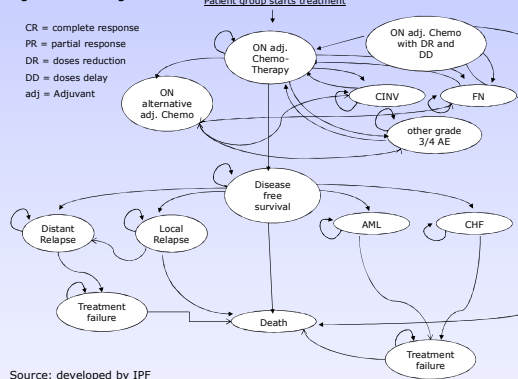
Objectives

As health economic data for well established adjuvant chemotherapy regimens in breast cancer patients like **anthracycline based regimens** rarely exists, this analysis addresses the cost-effectiveness of these treatment options **compared to a taxane-containing regime**. The combination of doxorubicin and cyclophosphamide (AC) has been a standard adjuvant breast cancer regime. The purpose of this analysis was to estimate the cost-effectiveness of AC, CMF (cyclophosphamide, methotrexate and 5-fluorouracil) and FEC (5-fluorouracil, epirubicin and cyclophosphamide) compared with AT (doxorubicin and docetaxel) administered as adjuvant therapy to women with node-positive early breast cancer in Spain. Long-term costs and consequences have been evaluated (beyond DFS and OS from clinical trials) to highlight the value for money of the chosen comparators.

Methods

We developed a multi-country Cost-Utility-Model to simulate the long-term consequences from initiation of adjuvant chemotherapy over ten years. Markov-modeling techniques were used to estimate the incidence of complications during chemotherapy (febrile neutropenia, chemotherapy-induced nausea/vomiting, dose reduction, dose-delay, other grade 3/4 adverse-events) and long-term consequences like local or distant relapse, acute myelogenous leukemia, chronic heart failure and death. Monte-Carlo simulation accounted for uncertainty. The model comprises 14 health states, with a cycle length of 3 months. Transition probabilities were derived from clinical and epidemiological studies; direct costs (2010 Euro) from published sources. The present economic evaluation was conducted from the perspective of the health care system.

Fig. 1: Model Design



Source: developed by IPF

Cohort definition

Patients with a mean age of 50 years entered the model after surgery and start with the adjuvant AT, AC, CMF or FEC chemotherapy. The cohort is defined as 1,000 women with primary operable breast cancer (mastectomy or breast-conserving surgery/lumpectomy), at least one histological verified positive axillary node. Included subgroups are: (A) triple negative patients, (B) estrogen receptor-positive patients and (C) progesterone receptor-positive patients.

Results

Over a 10-year timeframe, costs and QALYs, LYs associated to AT amounts to 15,361.89 € and 5.85 QALYs (6.50 LYs). Costs, QALYs and LYs associated with AC are 13,265.88 € and 5.85 QALYs (6.49 LYs). The cost-saving potential associated to AC amounts to 2,096.01 € per patient with comparable outcomes to AT.

Costs, QALYs and LYs associated with CMF are 14,144.63 €, 5.8 and 6.4 years, resp. AC dominates also CMF. FEC associated total cost are 15,138.23 € and dominates AT. FEC QALY gain is 0.18 QALYs (0.31 LYs) vs. AT.

Tab. 1: Results of costs QALYs and LYs

Strategy	Costs C	Diff. ΔC	QALYs E	Diff. QALYs ΔE	ICER
AT	15,361.89 €		5.8485		
AC	13,265.88 €	-2,096.01 €	5.8475	-0.0010	vs AT 2.1 mill €
CMF	14,144.63 €	-1,217.26 €	5.8410	-0.0075	vs AT 0.16 mill €
FEC	15,138.23 €	-223.66 €	6.0255	0.1770	FEC dominant vs AT
Strategy	Costs C	Diff. ΔC	LYs E	Diff. LYs ΔE	C per LYs gained
AT	15,361.89 €		6.5012		
AC	13,265.88 €	-2,096.01 €	6.4867	-0.0146	vs AT 143 k €
CMF	14,144.63 €	-1,217.26 €	6.4293	-0.0719	vs AT 16 k €
FEC	15,138.23 €	-223.66 €	6.8143	0.3130	FEC dominant vs AT

Source: IPF own calculations

ICER = incremental cost effectiveness ratio

Over a 10-year timeframe, AC, CMF and AT lead to fewer cases of AML: 1.75 per 100 patients vs 2.8 when FEC is used. FEC leads to fewer cases of local and distant relapses: 10 local relapse per 100 patients vs 15 (other treatments) and 15 distant leaps per 100 FEC treated patient vs 21-23 with other treatments.

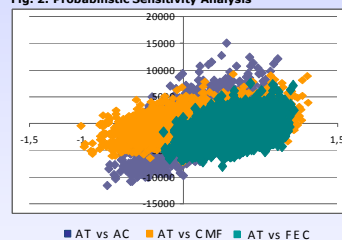
Tab. 2: Total costs broken down by its costs components

Cost components	AT	AC	CMF	FEC
Adjuvant CT	3,823.87 €	1,779.86 €	2,089.51 €	5,520.98 €
Alternativ CT and DR	13.43 €	32.03 €	38.70 €	35.62 €
Local relapse	478.49 €	452.54 €	435.49 €	322.94 €
Distant relapse	10,323.06 €	10,256.58 €	10,928.16 €	8,068.07 €
AML	658.20 €	635.57 €	637.19 €	1,083.79 €
CHF	64.83 €	109.31 €	15.56 €	106.83 €
Total	15,361.89 €	13,265.88 €	14,144.63 €	15,138.23 €

Source: IPF own calculations

The probabilistic sensitivity analyses show the robustness of the model.

Fig. 2: Probabilistic Sensitivity Analysis



Source: IPF own calculations

Monte-Carlo probabilistic sensitivity analysis, results of 5,000 trials plotting incremental cost versus incremental effects, demonstrated that AC is cost effective compared to AT in more than 70% of the simulations with a willingness to pay of 20,000 €; CMF in 60% and FEC in 63% of all simulations (Fig. 2).

Conclusion

The analysis demonstrates that AC, CMF and FEC chemotherapy were cost-effective alternative compared to AT. AC and CMF are associated with a clear cost advantage and comparable quality-of-life and life years. FEC leads to a higher quality of life and life years gained. From a health economic perspective, replacing cyclophosphamide by a taxane shows no additional value for money in the setting of adjuvant chemotherapy in breast cancer patients. From a cost-minimization viewpoint AC remains the dominant strategy up to a price of 0.15€/mg (current price is 0.01€/mg)."

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Additional Literature with the author

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