The CHEUAL Breast Cancer Model Application – Interactive Cost-Utility Analysis of Bevacizumab plus Paclitaxel in Metastatic BC to Support Decision Making: A Portuguese clinical perspective

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Backgound

Breast cancer is associated with a high prevalence, incidence and mortality all over the world (of 0,83%, 0,07% and 0,028% of Portuguese female population, respectively, WHO - Globocan 2008 and HEO 2008), representing a huge burden on individuals and health systems. The CHEUAL BC model is an economic evaluation interactive tool that makes inferences about future direct costs and health outcomes, providing an Incremental Cost per Quality-Adjusted Life Year (QALY) Ratio, capable of supporting clinical, hospital formulary drug inclusion and reimbursement decision-making, allowing the identification of breast cancer management strategies and treatments that are *good value for money* in a transparent and efficient way, in real time.

Objective

To evaluate the cost-utility of a new treatment option for metastatic breast cancer, Bevacizumab in association with Paclitaxel (still in Stage IV in Portugal), from the Portuguese clinical perspective, for better BC management.

Methods

The CHEUAL BC model was used to estimate costs and consequences of receiving medical treatment with Bevacizumab plus Paclitaxel, in comparation with the therapy most commonly used in Portuguese IPO, determined by 200 therapeutical charts (Fig. 1 and 2). CHEUAL BC model contemplates a 6 stage Markov Decision Process, with 20 transition cycles of 6 month each (time horizon of 10 years), two age ranges (24-64 and ≥65 years) and 3 levels of history of disease associated with major therapy adverse effects (0,1 or 2 or more, namely cardiovascular (ACVE), pulmonary (APD), renal (ARF), hepatic (AHF), intestine (AD), reumathological (AA), hematological (AC) diseases and osteoporosis (Ost)). Adverse effects data were taken from EMEA and INFARMED SPCs (Table 1), costs (including drug preparation, administration and ambulatory day care visit for drug infusion per drug cycle, disease stage and major complication episodes costs, Tables 2 and 3) and consequences (based on a 5D-EQ questionnaire done through patients with BC disease stages III and IV, Tables 2 and 3) were taken from a systematic literature review and both were discounted at 5% per year. The survey was validated through one-way sensitivity analysis, also discounted 5%.

Fig 1: Metastatic BC: New therapy option (Stages III and IV)

Bevacizumab (3h IV, 650mg) 21 days cycle, 12 month + **Paclitaxel** (4h IV, 1105mg) 21days cycle, 4 month

74% $VEGF_{165}$+
88% HER2 +; ER -

Fig. 2a) Metastatic BC: 1st line most current therapy (Stage III)

Docetaxel (1-3h IV, 75mg) + **Doxorubicin** (<1h IV, 85mg) + **Cyclophosphamide** (<1hIV, 850mg) 21 days cycle, 6 month

HER2+
ER -

Trastuzumab 1-3h IV, charge 520mg, 300mg maintenance dose, 21 days cycle, 12 month

Fig. 2b) Metastatic BC: 2nd line most current therapy (Stage IV)

5-Fluorouracilo Bolus IV, 340mg/day 7 days per month, 6 month

TABLE 1: Major Side Effects

Drug	Major Side Effects
PACLITAXEL	APD, **ACVE**, AA, **AC**
BEVACIZUMAB	AA, **AC**, **AD**
DOCETAXEL, DOXORUBICIN CYCLOPHOSPH	ARF, ACVE, **AC**, **AD**
TRASTUZUMAB	APD, **ACVE**, AA, AC, **AD**
5FLUORURACIL	ACVE, AC

TABLE 2: Disease Stages Current Global Therapy Costs and Consequences

BC Stage	Discounted Costs	Disc QALYS Per patient
III	164.781,21 €	2,29
IV	19.510,61 €	0,28

TABLE 3: Disease Stages New Therapy Option Global Costs and Consequences

BC Stage	Discounted Costs	Disc QALYS Per patient
III	169.659,06 €	1,27
IV	35.362,46 €	0,07

Results

Base-Case Cost-Utility Results: According to the incremental cost per QALY Ratio resulting from the analysis, the current therapy resulted in a cost saving of 16.880,56 €/QALY per patient.

One-Way Sensitivity Analysis Results: The impact of variable ± 25% variation was identified to influence the Incremental cost per QALY ratio overall result, for New drug global direct costs, Personal history of disease, Patients age at diagnosis, Tumor stage, Current treatment drug costs, BC costs, BC QALYs, Country discount rate, Time horizon, Total Complication prevalence and AHF; ARF, APD, ACVD, AA, Ost, AC and AD had no significant influence on the overall result.

Conclusions

Bevacizumab plus Paclitaxel treatment led to a less cost-effective alternative compared with most current treatment used in BC metastatic patients in Portugal.

References

Globocan (2008) – *Female breast cancer EU statistics*; **International Agency on Research on Cancer** (IARC) - European Commission of Health and Consumer Protection, Directorate - Public Health and Risk Assessment.

HEO (Health European Observatory, 2008) – (2006); Statistical data (Data on file, accessed in September, 21st, 2010)

EMEA (European Medicines Agency – Science Medicines Health 2010) – European Assessment Reports (EPARs)

Infarmed (2010) – Resumos das Características dos medicamentos (RCM) [Summaries of Product Characteristics of drugs])

Mackey *et al.* (2009), Adjuvant targeted therapy in breast cancer; Cancer, Vol. 115; Issue 6; p. 1154-1168.

Dedes *et al.* (2009); Bevacizumab in combination with paclitaxel for HER-2 negative metastatic breast cancer: An economic evaluation; European Journal of Cancer; Vol. 45; p. 1397-1406.

Dranitsaris *et al.* (2009); Economic analysis of albumin-bound Paclitaxel for the treatment of metastatic breast cancer; Journal of Oncology Pharmaceutical Practice; Vol.15; p. 67-78.

Karnon *et al.* (2006); Cost-effectiveness of extended adjuvant Letrozole in postmenopausal women after adjuvant Tamoxifen therapy - The UK perspective; Pharmacoeconomics; Vol. 24; N.º 3; p. 237-250.