

COST-EFFECTIVENESS ANALYSIS OF EVEROLIMUS PLUS EXEMESTANE vs. BEVACIZUMAB PLUS PACLITAXEL AND BEVACIZUMAB PLUS CAPECITABINE FOR THE MANAGEMENT OF POSTMENOPAUSAL WOMEN WITH ER+BREAST CANCER

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Introduction

- Estrogen receptor positive (ER+) metastatic breast cancer (mBC) patients progressing on nonsteroidal aromatase inhibitors (NSAIs) are candidates for treatment with Everolimus (EVE) plus Exemestane (EXE) ¹.
- BOLERO-2 trial has shown that EVE plus EXE provides clinical benefit, regardless of ethnicity².
- Moving further, BC patients whose tumors have progressed on hormone therapy are candidates for chemotherapy³. Single agents such as Paclitaxel (PACL) and Capecitabine (CAPE) have shown activity in mBC⁴⁻⁹. Nonetheless, the addition of Bevacizumab (BEV) a Mab directed against all isoforms of vascular endothelial growth factor A in PACL or CAPE is of common practice and has been evaluated in clinical trials¹⁰⁻¹¹.
- However, in the recent climate of financial constraints it is particularly important to evaluate the effectiveness of new therapies in relation to their long-term costs relative to existing ones¹².

Objectives

The purpose of the present study was to conduct a cost – effectiveness (CE) analysis of EVE plus EXE versus BEV plus PACL and BEV plus CAPE which constitute established treatments in Greek healthcare setting.

Methods

- An existing Markov model consisting of three health states was adapted locally to reflect the natural progression of postmenopausal women with ER+/HER2- advanced BC from the public third party payer perspective .
- The analysis was conducted over a lifetime horizon in the course of 1- month cycle.
- Efficacy (i.e. progression free survival (PFS) and overall survival (OS)) and safety considered in the model was extracted from relevant randomized Phase III clinical trials ^{2;11;13-14}.
- Utility values were extracted from the literature¹⁵.
- Costs assigned to each health state reflect local drug acquisition cost, administration costs, pre- treatment medications, lab and imaging tests, prophylactic treatment medication, management of adverse events (Table 1). All cost reflect the year 2013.
- An incremental cost effectiveness ratio (ICER) per QALY gained was calculated.
- A willingness to pay (WTP) threshold of €36,000 per QALY gained was used in current analysis, based on the WHO guidelines (i.e. a treatment should be considered cost-effective if the ICER is between 1 or 3 times the GDP per capita of that country)¹⁶.
- Costs and outcomes that occurred beyond one year were discounted at a 3.5% annual rate which is the standard practice in Greece¹⁷.
- One-way sensitivity analyses (OWSA) undertaken to ascertain the key drivers of cost-effectiveness.
- Probabilistic sensitivity analysis (PSA) was undertaken to deal with uncertainty.

Results

EVE plus EXE vs. BEV plus PACL and BEV plus CAPE

- EVE plus EXE produced higher discounted survival by 0.28 and 0.21 LYs and larger discounted quality adjusted survival by 0.19 and 0.16 QALYs in relation to BEV plus PACL and BEV plus CAPE, respectively, (Table 2).
- EVE plus EXE was a less costly treatment regimen compared to both BEV plus PACL (by €7,171) and BEV plus CAPE (by €4,368).
- Both differences were mainly attributed to the lower drug acquisition and administration cost of EVE plus EXE compared to BEV plus PACL and to higher pre-progression cost related to the use of BEV+PACL and BEV+CAPE compared to EVE+EXE.
- EVE plus EXE seems to be a dominant alternative over BEV plus PACL and BEV plus CAPE in a lifetime horizon as the former is related with greater health benefit and lower total lifetime cost (Table 2).

One Way Sensitivity Analysis

- OWSA revealed that the results are mainly driven from the PFS and OS.
- EVE plus EXE was no further a dominant alternative, but still was a cost-effective option over BEV plus PACL when the OS of EVE plus EXE reduced by 50% (ICER: €14,827) and when OS of BEV plus PACL increased by 50% (ICER: €3,456).
- In the comparison of EVE plus EXE over BEV plus CAPE, the former was a cost-effective alternative when it's PFS and OS reduced by 50% (ICER: €4,006 and ICER: €17,845, respectively) and when the PFS and OS of BEV+CAPE increased by 50% (ICER: €127 and ICER: €9,388, respectively).

Probabilistic Sensitivity Analysis

- PSA confirmed the deterministic results. EVE plus EXE was a cost-effective alternative over BEV plus PACL and BEV plus CAPE at the WTP of 36,000 per QALY in 98.5% and 94.8% of cases .(Figures 1 & 2).

Conclusion

EVE plus EXE may be a dominant (more effective and less costly) alternative relative to BEV plus PACL and BEVA plus CAPE in treatment of ER+mBC patients failing initial therapy with NSAIs.

Acknowledgement

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Table 1: Cost per cycle per model state

	EVE plus EXE	BEV plus PACL	BEV plus CAPE
Total Pre-progression cost/cycle			
Drug Acquisition cost	€1,613	€2,501	€2347
Administration cost	€0	€261	€116
Pre-treatment cost medication	€0	€82.58	€36.69
Lab tests cost	€42.82	€52.41	€48.25
Imaging tests cost	€53.34	€53.34	€53.34
Prophylactic treatment cost	-	€274.72	€416.77
Adverse event cost (one off cost)	€62	€5	€1
Total post-progression cost/cycle	€1,057.41	€1,057.41	€1,057.41
End of life cost	€823	€823	€823

Figure 1: CEAs curves: EVE plus EXE vs BEV plus PACL

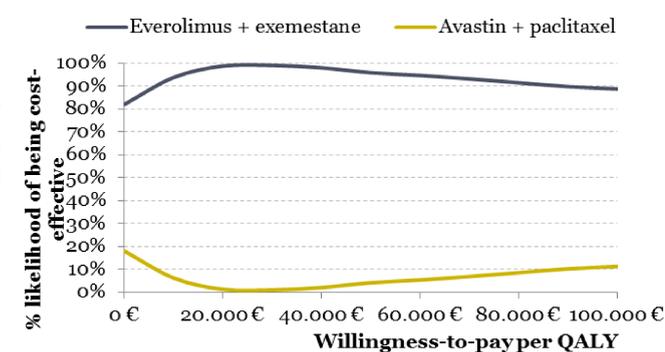


Figure 2: CEAs curves: EVE plus EXE vs BEV plus CAPE

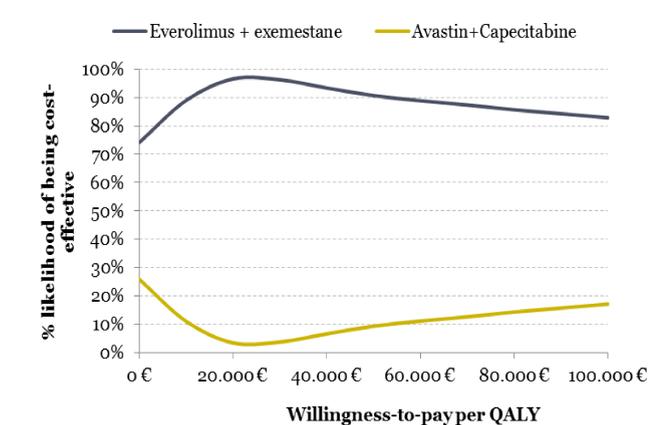


Table 2 :Results :EVE plus EXE vs BEV plus PACL and BEV plus CAPE

Outcomes	EVE plus EXE	BEV plus PACL	BEV plus CAPE
Treatment and administration costs	16,956 €	22,379 €	17,538 €
AE costs (grade 3/4)	62 €	5 €	1 €
Pre-progression background costs	1,000 €	3,744 €	3,946 €
Post-progression background costs	27,495 €	26,548 €	28,390 €
Terminal care costs	738 €	745 €	744 €
Total costs	46,251 €	53,422 €	50,619 €
QALYS: Pre-progressed	0.65	0.49	0,46
QALYS: Post-progressed	1.08	1.04	1,11
Total QALYS	1.72	1.53	1,57
Life years: Pre-progressed	0.88	0.68	0,59
Life years: Post-progressed	2.17	2.09	2,24
Total discounted life years	3.04	2.77	2,83
Incremental cost per QALY (EVE plus EXE vs comparator)		Dominant	Dominant
Incremental cost per LY (EVE plus EXE vs comparator)		Dominant	Dominant
Net monetary benefit		14,042 €	10,030 €

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