PCN117

A Cost Effectiveness analysis of Everolimus plus Exemestane compared to chemotherapy agents for the treatment of ER+ HER2- Metastatic Breast Cancer in the United Kingdom

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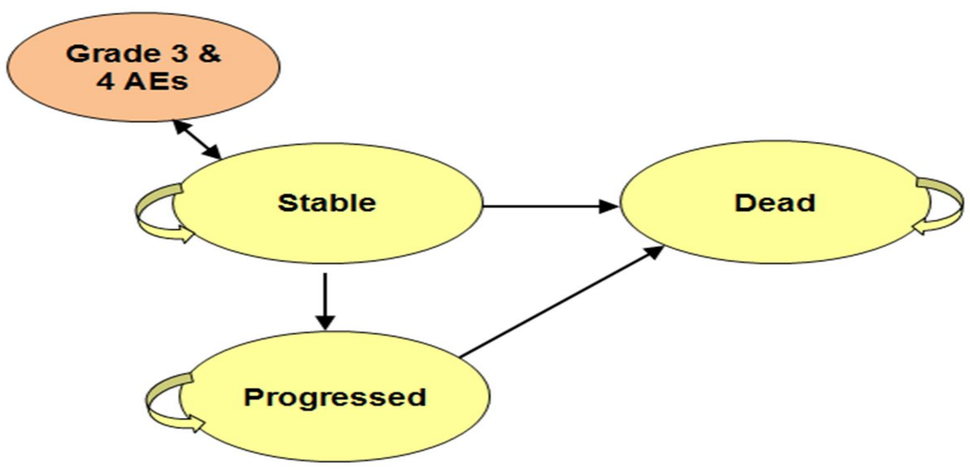
Background & Objectives

This study evaluated the cost-effectiveness of everolimus + exemestane (EVE+EXE) versus commonly used chemotherapy agents [docetaxel (DOC), vinorelbine (VIN), doxorubicin (DOX) and capecitabine (CAPE)] in patients with hormone receptor positive, HER2 negative advanced or metastatic breast cancer in the United Kingdom. This analysis is based on final Overall Survival data from the BOLERO-2 trial.

Methods

A partitioned survival model with monthly cycles was developed to compare treatment with EVE+EXE versus DOC, VIN, DOX and CAPE in patients with ER+ HER2- metastatic breast cancer over a 10-year time horizon from a UK NHS perspective. Three health states were modelled: stable disease, progressed disease and death. Patients moved between health states according to the model structure outlined in Figure 1.

Figure 1: Model structure



Progression-free survival (PFS) and overall survival (OS) for EVE+EXE were estimated from the BOLERO-2 trial. Log-logistic functions were used to extrapolate trial data beyond the follow-up period (Figure 2). In the absence of head-to-head evidence comparing EVE+EXE versus chemotherapy a naïve chained comparison was conducted with the link between EVE+EXE established via tamoxifen using the Bucher method. This analysis is documented elsewhere (Vieira et al 2013). A class effect was assumed for the four chemotherapy agents (Table 1).

Figure 2: Log-logistics curves for PFS and OS

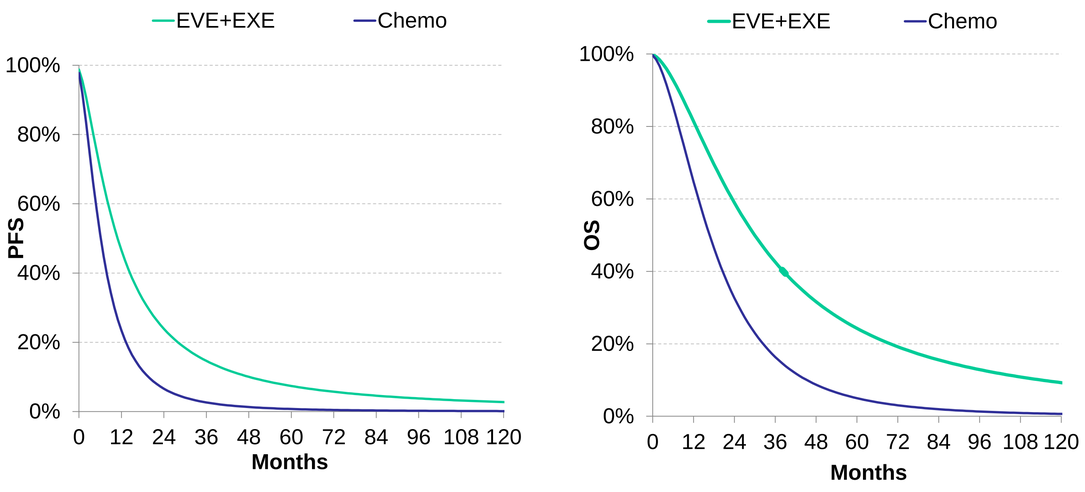


Table 1: Hazard ratios versus everolimus in combination with exemestane

	PFS	OS
Everolimus in combination with exemestane	**1.00**	**1.00**
Docetaxel (DOC)	1.85	2.09
Vinorelbine (VIN)	1.85	2.09
Doxorubicin (DOX)	1.85	2.09
Capecitabine (CAPE)	1.85	2.09

Note: hazard ratios (HRs) refer to the risk of the event, ie progression or death. In this particular analysis a high HR represents an increased risk of an event and therefore decreased PFS/OS for the comparator. Therefore a HR > 1 indicates worse effectiveness of the comparator treatment compared with everolimus in combination with exemestane.

Presented at the ISPOR, 17th Annual European Congress, Amsterdam , 8-12 NOV 2014

Table 2: Model inputs

Health state	**Utility**	**Source**
Stable	0.798	Lloyd et al.(2006)
Progressed	0.496	Lloyd et al.(2006)
Dead	0.000	Assumption
Health state	**Cost (per month)**	**Source**
Stable	£264.73	NICE CG81/PSSRU 2013
Progressed	£814.57	NICE CG81/PSSRU 2013
Terminal care (Dead)	£4,933.16	NICE CG81

Utilities from Lloyd et al. (2006) were adjusted for age and response and then combined with the PFS and OS trial data to calculate quality-adjusted life years (QALYs) associated with each treatment. Background health state and terminal care resource use were derived from NICE Clinical Guideline 81. Drug costs were taken from the British National Formulary.

Grade 3 and 4 adverse events (AEs) rates were obtained from the BOLERO-2 trial for EVE+EXE and from a prospective randomised trial for chemotherapy agents (Chan et al. 1999). These were applied as one-off events at the beginning of treatment. Patients experiencing an AE were assigned an event-specific disutility and incurred an event-specific cost. Disutilities were obtained from various sources in the literature (Lloyd et al. 2006, Nafees et al. 2008, Doyle et al. 2008). Costs were taken from NHS Reference Costs 2012-13. Discounting was applied to both costs and benefits at 3.5%.

Results

Over a ten year time horizon, EVE+EXE led to a life expectancy of 3.55 years, compared to 1.88 for chemotherapy agents (DOC, VIN, DOX and CAPE). EVE+EXE resulted in 2.06 QALYs, compared to 0.95 for chemotherapy agents. Total costs were £48,085 for EVE+EXE compared to £31,835 vs. DOC, £25,021 vs. VIN, £23,743 vs. DOX and £21,851 vs. CAPE. The incremental costs per QALY were £14,550 vs. DOC, £20,653 vs. VIN, £21,797 vs. DOX and £23,491 vs. CAPE. Results were most sensitive to changes in PFS for chemotherapy and disease related costs.

Table 3: Cost-effectiveness results for everolimus in combination with exemestane compared with chemotherapy agents

Everolimus in combination with exemestane compared with:	**Incremental costs**	**Incremental QALYs**	**ICER**
Docetaxel (DOC)	£16,249	1.116	£14,550
Vinorelbine (VIN)	£23,064	1.116	£20,653
Doxorubicin (DOX)	£24,342	1.116	£21,797
Capecitabine (CAPE)	£26,233	1.116	£23,491

Conclusions

This analysis suggests that EVE+EXE is a cost effective option compared with commonly used chemotherapy agents in UK clinical practice (DOC, VIN, DOX and CAPE). Patients treated with EVE+EXE have a better quality of life (2.06 QALY) compared to patients treated with chemotherapy agents (0.95 =QALY) which is not only due to the better efficacy profile of EVE+EXE but also due to the better AEs profile of endocrine therapy.

References

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6.Chan *et al.* (1999). Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. *J Clin Oncol,* 17: 2341-2354.

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