Cost-Utility Analysis of Elacestrant versus Standard of Choice in ER+/HER2- Advanced Breast Cancer Patient from US Healthcare Payer Perspective

EE455

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Objectives

To assess the cost-effectiveness of elacestrant compared to standard endocrine therapy in second-line treatment for estrogen receptor-positive (ER+) and human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer from the US payer perspective

Methods

> **Model type:** Three-state partitioned survival model with mutually exclusive health states: progression-free, post-progression, death

> **Intervention:** Elacestrant (ELA) administered orally once daily

> **Comparators:** Intramuscular injection of 500 mg fulvestrant on days one and day 15, followed by monthly injections thereafter, or orally administered anastrozole 1 mg, letrozole 2.5 mg, or exemestane 25 mg once daily (SOC)

> **Targeted population:** Postmenopausal women with ER+/HER2- metastatic breast cancer progressing during or after treatment with one or two prior lines of endocrine therapy

> **Perspective:** US healthcare sector
> **Time horizon:** Lifetime (20 years)
> **Cycle length:** 1 month
> **Discount rate:** 3%

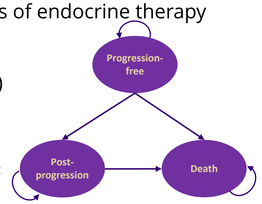


Figure 1. Model Schematic

> **Survival parameters:**
Clinical efficacy data from the EMERALD phase III randomized clinical trial publication were used to derive the survival parameters used in the mode.[1]

- We digitized the Kaplan-Meier (KM) curves from the SOC arm using WebPlotDigitizer and applied the algorithm by Guyot et al. to generate estimates of individual patient data(IPD).[2]
- We fit the following parametric survival distributions to the IPD data: Exponential, GenGamma, Gompertz, Loglogistic, Lognormal, Weibull.
- We selected generalized gamma distribution for PFS and lognormal distribution for OS based on the Akaike information criterion (AIC), visual inspection, and clinical plausibility. Statistical analysis was carried out in R 4.1.3.
- We tested the parallel hazard assumption using the reconstructed KM curves, confirming their parallel nature. Then, we applied the HRs observed in the EMERALD trial to the PFS and OS curves in the SOC arm to derive the survival estimates for the ELA arm.

Model inputs

Table1. Model inputs: base-case, lower value, upper value, distribution and reference

Variables	Base-Case	Lower Value	Upper Value	Distribution	Reference
Survival parameters					
SOC PFS curve mu	0.929	0.768	1.089	GenGamma	Bidard et al.
SOC PFS curve sigma	0.811	0.73	0.91	GenGamma	Bidard et al.
SOC PFS Q	-0.402	-0.71	-0.09	GenGamma	Bidard et al.
SOC OS curve meanlog	3.099	2.86	3.37	Log-normal	Bidard et al.
SOC OS curve sdlog	1.153	0.97	1.37	Log-normal	Bidard et al.
Hazard ratio for PFS	0.700	0.55	0.88	Log-normal	Bidard et al.
Hazard ratio for OS	0.750	0.54	1.04	Log-normal	Bidard et al.
Cost(per cycle)					
Elacestrant drug cost	$19,182	$15,307	$23,057	Gamma	IBM® Micromedex® RED BOOK®,VAFSS
Fulvestrant drug cost	$177	$110	$244	Gamma	ASP+6% ;VAFSS
Anastrozole drug cost	$5	$4	$6	Gamma	NADAC, +- 20%
Letrozole drug cost	$4	$3	$5	Gamma	NADAC, +- 20%
Exemestane drug cost	$25	$20	$30	Gamma	NADAC, +- 20%
IV administration cost	$355	$284	$426	Gamma	Kruse et al. 2008
Outpatients visit	$243	$195	$292	Gamma	Sorensen et al. 2012
Cost after disease progression(3rd line therapy)	$9,411	$7,529	$11,293	Gamma	Sorensen et al. 2012
SOC expected AE cost	$ 25	N/A	N/A	N/A	Assumption
ELA expected AE cost	$ 45	N/A	N/A	N/A	Assumption
Cost(per episode)					
Nausea	$9,098	N/A	N/A	N/A	McGregor et al. 2023
Fatigue	$9,618	N/A	N/A	N/A	McGregor et al. 2023
Vomiting	$9,098	N/A	N/A	N/A	McGregor et al. 2023
Arthralgia	$7,851	N/A	N/A	N/A	McGregor et al. 2023
Diarrhea	$9,325	N/A	N/A	N/A	McGregor et al. 2023
Back pain	$3,192	N/A	N/A	N/A	Donga et al. 2017
Headache	$9,006	N/A	N/A	N/A	McGregor et al. 2023
Utilities					
Progression-free	0.72	0.58	0.86	Beta	Lloyd et al. 2006
Progressed	0.44	0.35	0.53	Beta	Lloyd et al. 2006
AE disutility for SOC per cycle	-2.32E-05	N/A	N/A	N/A	Assumption
AE disutility for ELA per cycle	-4.19E-05	N/A	N/A	N/A	Assumption
Other parameters					
Discount, costs & outcomes	3%				

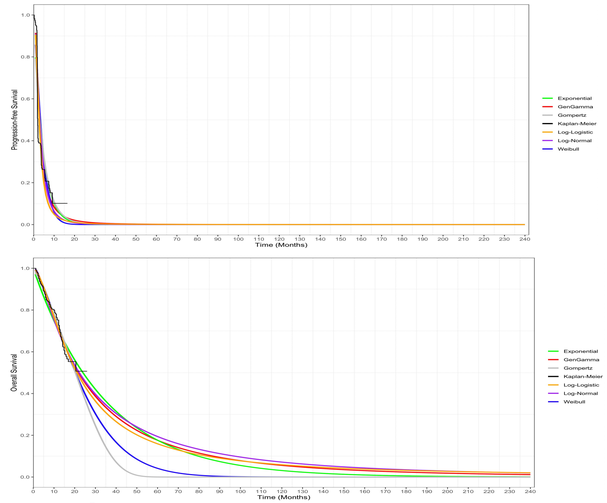
Costs:
- Drug acquisition costs were obtained from IBM® Micromedex® RED BOOK®, VA Federal Supply Schedule price, and CMS Average Sales price.
- IV administration costs, outpatient visit costs, costs after progression, and adverse events costs were derived from the published literature.
- All costs were inflated to 2024 US dollars.

Outcomes: Quality-adjusted life years (QALYs) for PF and PP and decremental QALYs for AEs were obtained from the published literature.

Sensitivity Analyses: One-way deterministic sensitivity analyses and probabilistic sensitivity analyses were conducted to test model robustness.

Subgroup Analyses: We performed subgroup analyses for the ESR1 mutation population based on the survival curves from the EMERALD trial.[1]

Figure 2. Six parametric distributions fit to reconstructed progression-free Survival(top) and overall survival(bottom) curves in the SOC arm; **generalized gamma** distribution for PFS, and **lognormal distribution** for OS



Result

Strategy	Total Cost	Total QALYs	Incremental Cost	Incremental QALYs	ICER	Cost-effectiveness probability at $150,000 WTP
Base-case						
SOC	$332,556	1.56				
ELA	$580,340	2.18	$247,784	0.63	$393,405 /QALY	10.6%
Subgroup Analyses : ESR1 mutation population						
SOC	$263,435	1.32				
ELA	$697,977	2.50	$434,542	1.19	$366,562 /QALY	4.2 %

Table2. Deterministic result from the base case analysis and subgroup analysis

> **Base-case result:** Total QALYs for ELA and SOC were 2.18 and 1.56, respectively, with corresponding total costs of $580,340 and $332,556. The ICER was $393,405 per QALY.

> **Sensitivity analyses result:**
- For the one-way sensitivity analysis, the input parameters with the most influence on the ICER were OS hazard ratio, progressed utility, and ELA drug cost.
- PSA estimated that ELA had a 10.6 % chance of being cost-effective at a WTP of $150,000/QALY.

> **Subgroup analyses result:** For the ESR1 mutation population, total QALYs for ELA and SOC were 2.5 and 1.32, respectively, with corresponding total costs of $ 697,977 and $263,435. The ICER was $366,562 per QALY.

Figure 3. Incremental cost-effectiveness ratio tornado diagram for multiple 1-way sensitivity analyses

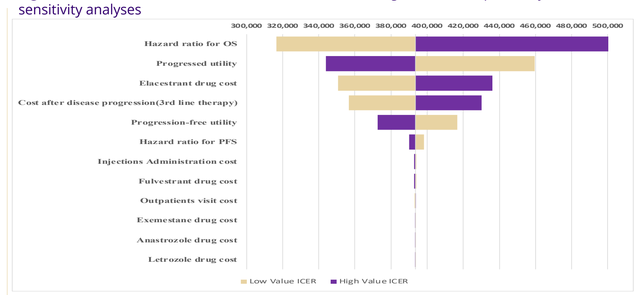


Figure 4. Cost-effectiveness acceptability curve

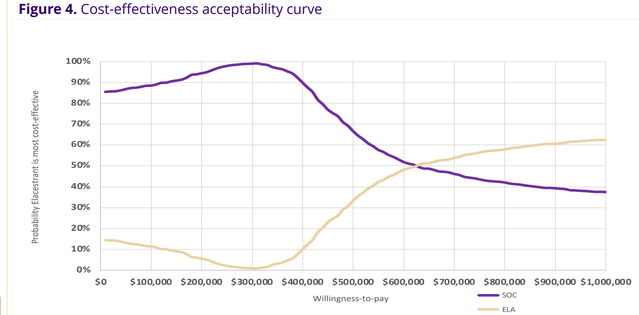
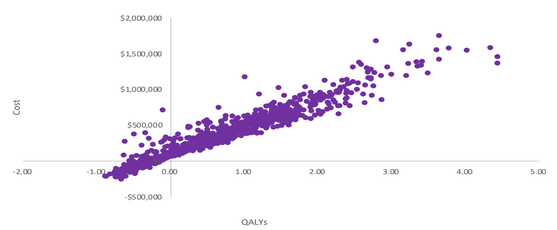


Figure 5. Incremental Cost-effectiveness scatter plot



Conclusion

At the willingness-to-pay threshold of $150,000 per QALY, elacestrant is not cost-effective as a second-line treatment for ER+/HER2- advanced breast cancer.

Reference

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2. Guyot P, Ades AE, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. BMC Med Res Methodol. 2012;12:9. Published 2012 Feb 1. doi:10.1186/1471-2288-12-9