Cost-effectiveness analysis of early versus delayed use of abemaciclib combination treatment in patients with high-risk HR+/HER2- early breast cancer: A US payer perspective

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Introduction

- Abemaciclib combined with fulvestrant is a first-line treatment for patients with hormone receptor-positive (HR+)/ human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (MBC).
- New indication of abemaciclib plus endocrine therapy in treating HR+/ HER2- early breast cancer (EBC) at high risk of recurrence was approved by the FDA and recommended as first-line treatment by clinical guidelines.

Objective

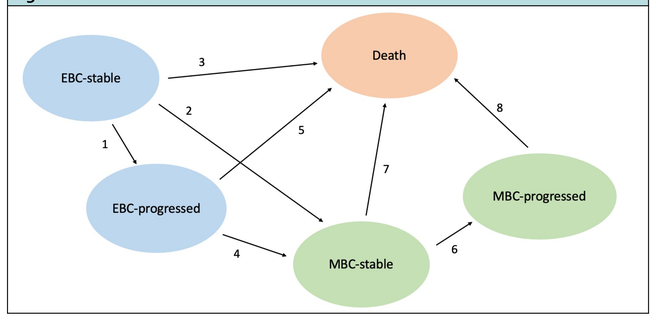
- To evaluated the cost-effectiveness of early use of abemaciclib and ET combination as first-line therapy and then use of fulvestrant after developing MBC (early use) versus ET treatment in EBC followed by delayed use of combination abemaciclib and fulvestrant in MBC (delayed use).

Method

- **Perspective**
  - Payer in the U.S. healthcare system
- **Model** (**Figure 1**)
  - 6 months per cycle Markov model using Microsoft Excel 365
  - 10-year time horizon
  - Both 3% discounted rate and half-cycle correction
- **Treatment design** (**Figure 2**)
  - Assumptions were based on two clinical studies, monarchE and MONARCH 2
- **Patient population**
  - Aged 51 and previously received definite surgery
  - Diagnosed with HR+/HER2- EBC
  - At high risk of recurrence*
- **Outcomes**
  - Quality-adjusted life year (QALYs)
  - Incremental Cost-Effectiveness Ratio (ICER)
- **Sensitivity analysis**
  - Deterministic and probabilistic sensitivity analysis
- **Parameter inputs** (**Table 1**)

***High risk of recurrence**
1. Ki-67 index ≥ 20%
2. ≥ 4 positive axillary lymph nodes (ALN) involvement or with 1-3 ALNs plus either grade 3 disease or tumor ≥ 5 cm

Figure 1. Markov model



Method

Figure 2. Treatment design

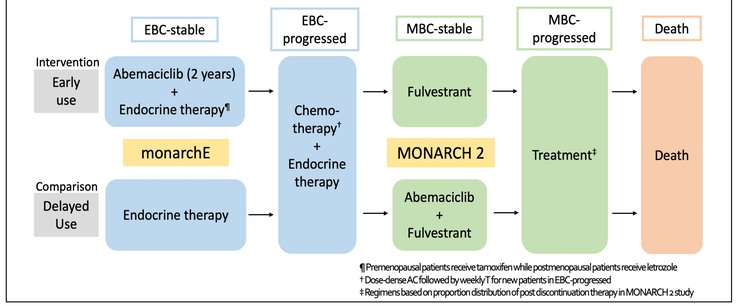


Table 1. Parameter inputs

No	Type	Study	Outcome
Transitional probabilities			
1	Dynamic	monarchE	Invasive disease-free survival
2			Distant relapse-free survival
3		Observational	Overall survival
6		MONARCH 2	Progression-free survival (PFS)
7			Overall survival
8	Fixed	Observational	Distant disease-free survival
4		Observational	Overall survival
5			

Variable	Cost	Duration
Costs§		
Abemacilcib	$16,531	month
Endocrine therapy	$525	month
Fulvestrant	$2,327	month
Dose-dense AC followed by weekly T	$1,148	cycle
Chemotherapy	$3,394	month
Endocrine treatment	$493	month
Target therapy	$4,720	month
Non-drug	$904	one time

Health state	Value
Utility values	
EBC-stable	0.860
EBC-progressed	0.767
MBC-stable	0.540
MBC-progressed	0.443
Death	0

Adverse event	Cost	Disutility value
Adverse events		
Diarrhea	2288	-0.1198
Constipation	3688	-0.0056
Vomiting	1013	-0.04802
Alopecia	0	-0.0891
Nausea	2978	-0.1214
Rash	1708	-0.03248
Neutropenia	4895	-0.2466
Anemia	5926	-0.1914
Thrombocytopenia	6461	-0.108
Urinary tract infection	2826	-0.2303
Venous thromboembolic event	23951	-0.1

§ Cost adjustment: 3% inflation rate to 2022 U.S. dollar

Results

- **Simulation results** (**Table 2**)
- **ICER**
  - **$168,112 per QALY gained** in early compared with delayed use group
  - Willingness-to-pay (WTP) threshold: $150,000/QALY
  - Early use of abemacilcib combination therapy is not cost effective

Table 2. Base case

Treatment	Cost	Net Cost	QALY	Net QALY	LY	Net LY
Early use	$295,813	$134,657	6.513	0.801	8.386	0.614
Delayed use	$161,156		5.712		7.772	

Results

- **Deterministic sensitivity analysis (DSA)** (**Figure 3**)
  - Results were most sensitive to cost of abemaciclib
  - Price reduction of abemaciclib
    - 10% reduction will be cost effective under $150,000/QALY WTP
- **Probabilistic sensitivity analysis (PSA)** (**Figure 4**)
  - 50% of being cost effective in early use under $150,000/QALY WTP

Figure 3. DSA

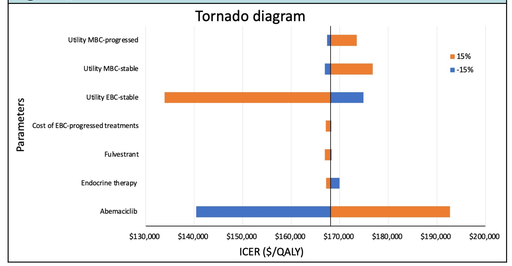
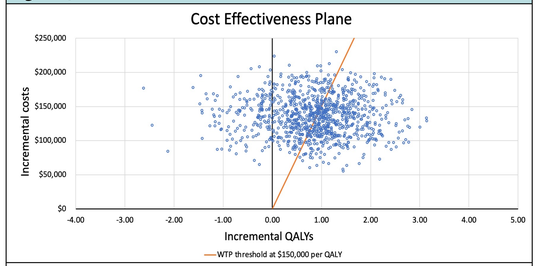
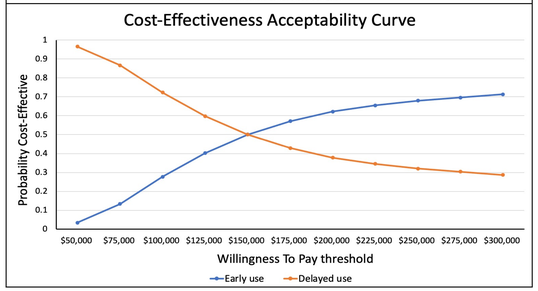


Figure 4. PSA





Discussion

- **Base case**
  - Huge cost difference was observed
    - High drug cost: abemaciclib ($99,187 per cycle, $16,531 per month)
    - More patients in the early use group stay in EBC-stable state in the first 24 months
  - Good clinical outcome: over a half QALY and half life-year gained in early use patients
- **Sensitivity analyses**
  - Utility in MBC-stable state
    - Significant differences of progression-free survival (PFS) and overall survival (OS) in two arms from the MONARCH 2 study
- **Strength**
  - First study on economic evaluation of abemaciclib combination therapy in EBC
  - Simulate the whole disease process of breast cancer: EBC → Death
  - Evaluation on different timing of using first-line abemaciclib combination therapy
- **Limitations are from the study assumptions**
  - Backbone therapy for HR+/HER2- patients
    - We assumed endocrine treatment should be given in each state
  - Abemaciclib combination therapy
    - As first-line treatment either in early or metastatic stage (Early vs. Delayed use)
  - Combination of multiple studies
    - Fail to fully identify the treatment effect of early using abemaciclib combination therapy

Conclusion

Abemaciclib combination therapy in early compared with delayed use is not cost effective at $150,000 willingness-to-pay threshold