Cost-effectiveness Analysis of Capivasertib Plus Fulvestrant in Hormone Receptor (HR)-Positive, Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Advanced Breast Cancer: a US Payer Perspective

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Background

- CDK4/6 inhibitor (CDK4/6i) in combination with fulvestrant or aromatase inhibitors is current standard of care for HR+ advanced breast cancer (ABC) per the NCCN guideline[1]
- Many patients develop disease progression from endocrine resistance due to systemic PI3K/AKT/mTOR activation, leading to progression-free survival (PFS) of less than 6 months[2-4]
- FAKTION and CAPItello-291 trials demonstrated that the addition of capivasertib (an oral AKT inhibitor), as part of a second-line treatment strategy, to fulvestrant resulted in significantly improved PFS as compared to fulvestrant alone for the treatment of HR+/HER2- ABC[5,6]
- However, the economic value of the combination therapy has not been evaluated to date

Objective

- To examine the cost-effectiveness of capivasertib plus fulvestrant versus fulvestrant monotherapy in patients with HR+/HER2- ABC who had disease progression during or after previous endocrine therapy in the US healthcare setting

Methods

- Patient Population:
  - Patients with HR+/HER2- ABC who had disease progression during or after previous endocrine therapy, with or without previous CDK4/6i
- Intervention & Comparator:
  - Capivasertib + fulvestrant vs. fulvestrant monotherapy
  - The choice of comparator was based on the clinical trials[5,6]
- Model Structure, Health States, Time Horizon & Perspective:
  - A partitioned survival model with three health states, progression-free disease (PFD), progressive disease (PD), and death, over a 5-year time horizon from a US payer's perspective
- Clinical Data:
  - PFS and overall survival (OS) data were derived from FAKTION trial[5]
  - The best-fit model was determined based on Akaike information criterion (AIC) goodness-of-fit statistics[7] and visual inspection (Figure 1)
- Cost & Utility Data:
  - Utility, disutility, and cost data were obtained from published literature and Centers for Medicare and Medicaid Services (CMS)[8-17] (Table 1)
  - Capivasertib cost was estimated based on the median wholesale acquisition cost (WAC) for newly approved drugs in ABC[18]
  - Costs were presented in 2023 US dollars
  - Both costs and effectiveness were discounted by 3%
- Analyses:
  - ICER ($ per QALY gained) was calculated and compared with a WTP threshold of $150,000 per QALY
  - One-way and probabilistic sensitivity analyses and scenario analysis were performed to examine parameter uncertainty

Figure 1. Kaplan-Meier Curves and Parametric Distributions for PFS and OS in Overall Population

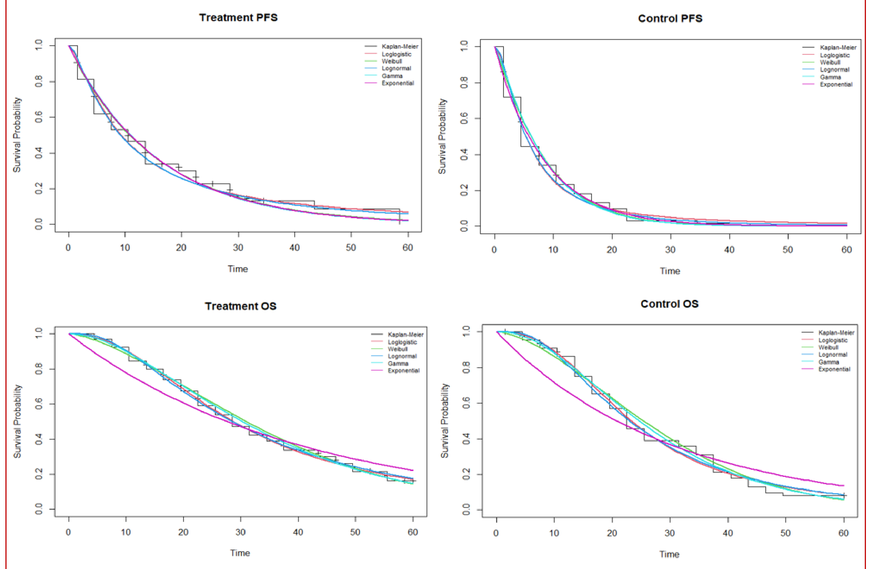
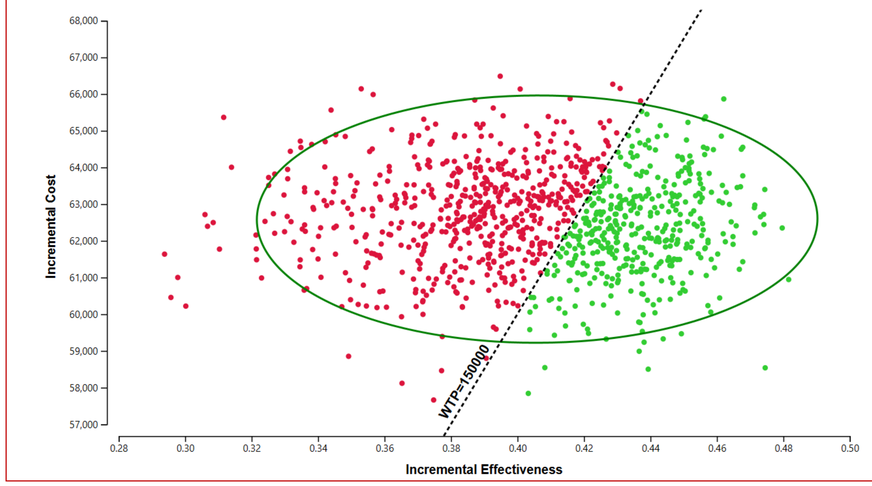


Table 1. Input Parameters for Base Case Analysis

Parameters	Estimates	Parameters	Estimates	Parameters	Estimates
Utility Values		**Medications Costs (per cycle)**		**AEs (grade ≥ 3) Management Costs (per event)**	
PFD	0.85	Fulvestrant (1st cycle)	$334	Diarrhea	$4,005
PD	0.44	Fulvestrant (following cycle)	$167	Rash	$1,908
Disutility Values		Capivasertib	$5,141	Infection (all)	$16,123
Diarrhea	-0.01	Other costs including IM fulvestrant administration costs, medical follow-up costs, further 3rd-line chemotherapy costs, palliative care costs, and terminal care costs were also included in the analysis based on the treatment cycle			
Rash	-0.0027				
Infection (all)	-0.0192				

AEs, adverse events

Figure 2. Cost-effectiveness Scatterplot



Results

- Capivasertib +fulvestrant was more effective (1.71 vs. 1.30 QALYs) and more costly ($312,295 vs. $249,697) than fulvestrant monotherapy, resulting in an ICER of $152,678 per QALY gained (Table 2)
- The monthly cost of capivasertib ($5,141) had the largest impact on the ICER (not shown)
- At the WTP of $150,000, the probability that capivasertib + fulvestrant being cost-effective was 41% (not shown)
- To reach a 90% probability, the monthly cost of capivasertib must decrease to $4,576 (90% of baseline price) at the same WTP threshold (Table 3)

Table 2. Base Case Result

Strategy	Category	Cost ($)	Incr. Cost ($)	Eff	Incr. Eff	ICER ($ per QALY gained)
Fulvestrant monotherapy	Undominated	249,697	-	1.30	-	-
Capivasertib + fulvestrant	Undominated	312,295	62,598	1.71	0.41	152,678

Table 3. Scenario Analysis Result

Variable	Baseline ($)	Change	Cost ($)	Monte Carlo Acceptability at WTP = $150,000
Monthly cost of capivasertib	5,141	Cut to 90%	4,576	90%

Eff, effectiveness; ICER, incremental cost-effectiveness ratio; Incr., incremental; QALY, quality-adjusted life-year; WTP, willingness-to-pay

Conclusion

- The combination of capivasertib + fulvestrant was not cost-effective compared to fulvestrant monotherapy for HR+/HER2- ABC patients at a $150,000 WTP threshold with a monthly cost of capivasertib at $5,141 in the US healthcare setting
- One of the limitations is that the clinical data in analyses were based entirely on efficacy findings in the FAKTION trial as there was no available real-world effectiveness data
- Further analyses will be conducted based on the FDA-approved indication (the PI3K/AKT/PTEN pathway-altered population)[19], the list price of capivasertib, and include other comparators that are standard of care for second-line HR+ ABC

References

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