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Cost-effectiveness analysis of ribociclib plus endocrine therapy for the treatment of HR+/HER2- Early Breast Cancer in Greece

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KEY FINDINGS & CONCLUSIONS

- Results of the study suggest that ribociclib plus endocrine therapy (ET) as treatment for patients with HR+/HER2- early breast cancer in Greece is likely to result in gains in QALYs compared with ET alone; as well as cost savings when compared to abemaciclib plus ET in the subgroup analysis.

INTRODUCTION

- The development and approval of the cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors have transformed the treatment of HR+/HER2- advanced or metastatic breast cancer (aBC). CDK4/6 inhibitors were evaluated in the adjuvant early breast cancer (eBC) setting.[1,2]
- The efficacy and safety of ribociclib plus ET as adjuvant treatment in patients with HR+/HER2- eBC was evaluated in the phase 3 multicenter, randomized, open-label NATALEE trial (NCT03701334).[1,3]

OBJECTIVE

- To assess the cost-effectiveness of ribociclib plus ET versus ET monotherapy as adjuvant therapy for patients with HR+/HER2– eBC from the Greek healthcare system perspective, according to the inclusion criteria and intervention in NATALEE trial.
- Additionally, a subgroup analysis comparing ribociclib+ET and abemaciclib+ET was performed for MonarchE-eligible patients.

BACKGROUND

- As of the April 29, 2024, data cut-off (DCO), in NATALEE trial, there were 263 events (10.3%) in the ribociclib plus ET arm and 340 (13.3%) in the ET only arm.[4]
- Ribociclib plus ET demonstrated a statistically significant improvement in the trial primary outcome, invasive disease-free-survival (iDFS) relative to ET monotherapy, with a hazard ratio (HR) of 0.72 (95% CI: 0.61-0.84).[4]
- MonarchE is an open-label, phase 3 trial investigating the addition of abemaciclib to ET for node-positive HR+/HER2- eBC patients at high risk of recurrence, based on clinicopathological characteristics.[2]

METHODS

- A semi-Markov cohort global model with 28-day cycles was adapted to simulate the clinical and economic outcomes in the Greek setting.
- The model is evaluated for the full population (NATALEE intent-to-treat [ITT] population)] as well as one additional subgroup [MonarchE-Eligible Population (MonarchE Cohort 1)].[2]
- Numbers of patients and estimates for iDFS are summarized by subgroup in **Table 1.**[4]

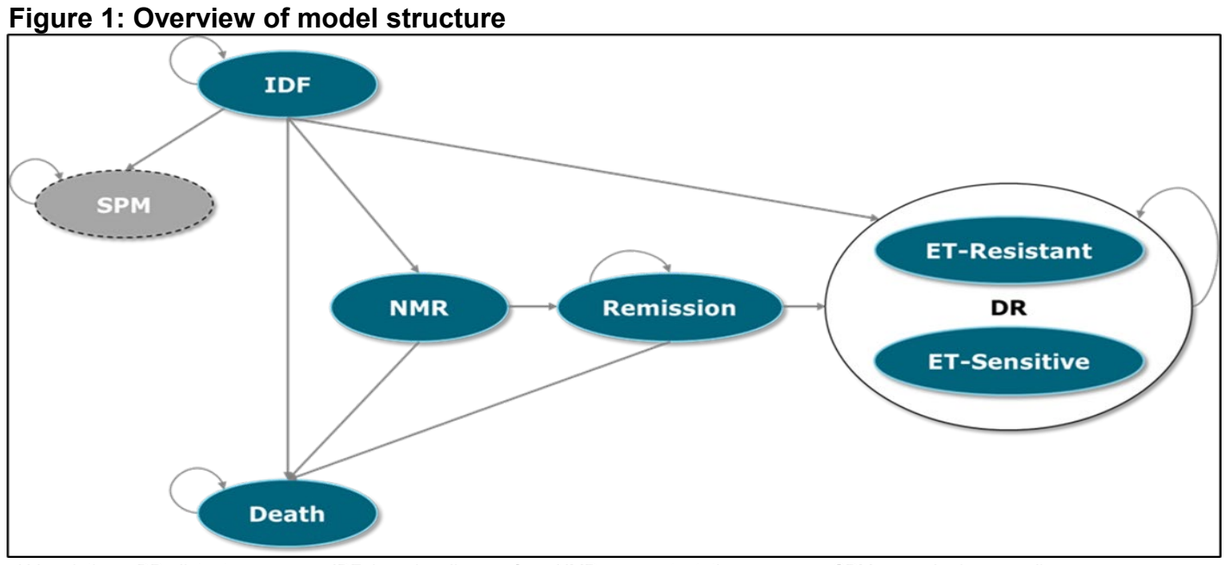
Table 1. Numbers of Patients and iDFS for NATALEE ITT population

	Number of Patients		iDFS Hazard Ratio (95% CI)
	Ribociclib + ET	ET	Ribociclib + ET vs. ET
Full Population (NATALEE ITT)	2549	2552	0.715 (0.609, 0.840)

Note: iDFS HR were extracted as raw data from NATALEE CSR.
Abbreviations: ET: endocrine therapy; iDFS: invasive disease-free survival; ITT: intent-to-treat population

- Six health states were captured in the model, presented in **Figure 1.**
- Patients entered in the iDFS state and transitioned based on time-dependent probabilities The iDFS was modeled using parametric survival models fitted to patient-level data from the NATALEE trial (DCO April 29, 2024).
- For abemaciclib plus ET, the iDFS was modeled by applying a hazard ratio from a matching-adjusted indirect comparison to the ribociclib plus curve.
- In the DR state, patients received subsequent treatment with fixed life years (LYs) and quality-adjusted life yeas (QALYs) based on MONALEESA-2/3 trial outcomes.[5,6]
- Direct costs (€, 2025) of different healthcare resources were considered and derived from official Greek sources.[7,8]
- Costs and clinical effects were discounted at 3.5 and 1.5% annually, respectively.[9]

Figure 1: Overview of model structure



Abbreviations: DR: distant recurrence, IDF: invasive disease-free; NMR: non-metastatic recurrence; SPM second primary malignancy

RESULTS

BASE CASE

- The deterministic ICER for ribociclib plus ET versus ET monotherapy was €19,502 per QALY gained, while the probabilistic ICER was €7,928, indicating a cost-effective treatment option.
- Ribociclib plus ET and ET monotherapy incurred the highest costs during the iDFS and DR phase, respectively. This reflects the longer event-free duration in the ribociclib arm and the greater need for subsequent treatment following relapse in the ET monotherapy arm.
- Total discounted lifetime costs and QALYs for ribociclib plus ET, ET monotherapy, and differences between the arms are presented in **Table 2.**

Table 2: Summary of Deterministic Cost-Effectiveness Results for ITT NATALEE Population

	Full Population (NATALEE ITT)	
Regimen Name	**Ribociclib + ET**	**ET**
Totals, discounted		
Costs, (€)	43,208	30,375
QALYs	13.56	12.90
Difference (Ribociclib + ET vs Comparator)		
Costs, (€)	12,833	
QALYs	0.66	
ICER (Ribociclib + ET vs Comparator)		
Cost per QALY saved	19,502	

Abbreviations: ET: endocrine therapy, ICER: incremental cost-effectiveness ratio; ITT: Intent-to-treat population; N/A: non-applicable; QALYs: quality adjusted life years

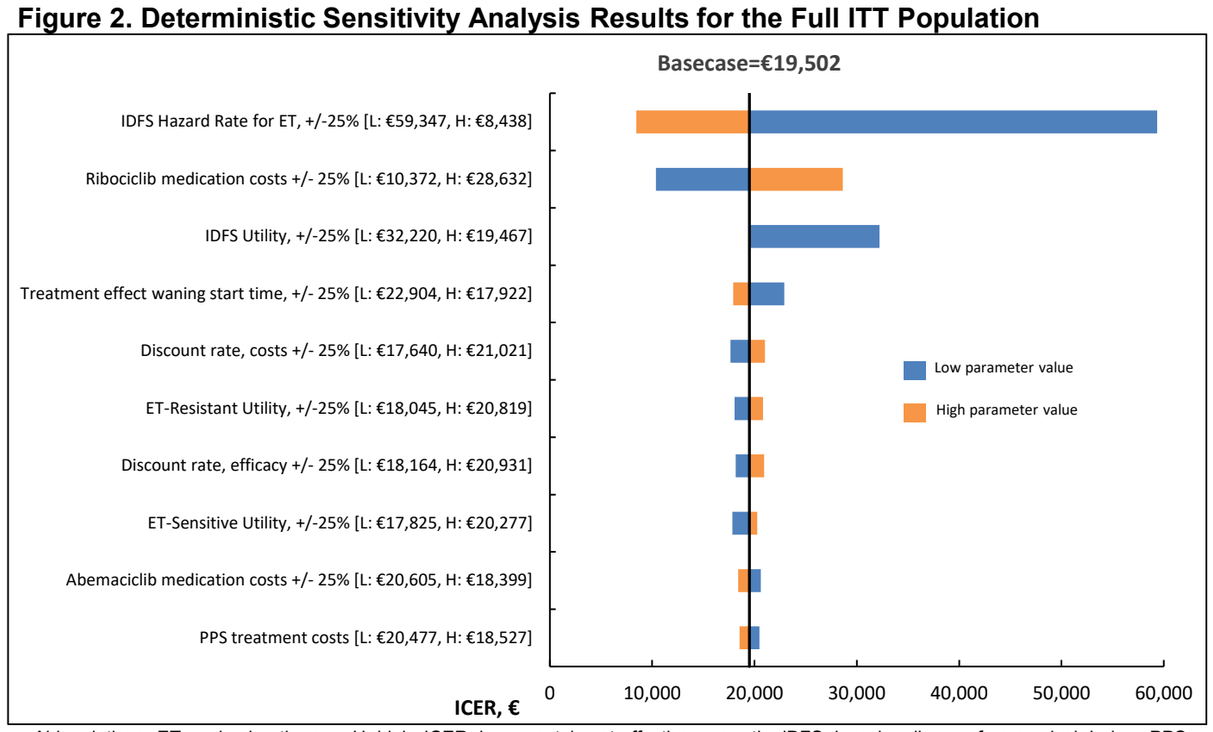
RESULTS (continued)

SENSITIVITY ANAYSES

Deterministic Sensitivity Analysis (DSA)

- In the base case, iDFS transition probabilities for ET were estimated from extrapolations of iDFS survival data for patients randomized to ET in the NATALEE trial.
- In the tornado analysis, the HR for ET was calculated by applying the estimated HR for ET versus ribociclib (**Table 1**) to the projected iDFS curve for ribociclib in the model. The HR for ET was varied by the lower and upper bounds of the corresponding 95% confidence interval.
- A tornado plot presenting the DSA results for the full ITT population for the ET monotherapy comparison is shown in **Figure 2**.
- The ICER per QALY gained was most sensitive to variations in iDFS hazard rates for ET, which resulted in an ICER of €59,347 for the lower bound and €8,438 for the upper bound.
- Parameters for which the results were sensitive included the medication cost for ribociclib, utility values for iDFS state and the discount rate applied to the efficacy outcomes.
- Relative to base ICER of €19,502, a +/-25% change in medication cost for ribociclib varied the ICER from €10,372 to €28,632 per QALY gained.
- Changing the iDFS utility value varied the ICER from €19,467 to €32,220 per QALY.

Figure 2. Deterministic Sensitivity Analysis Results for the Full ITT Population

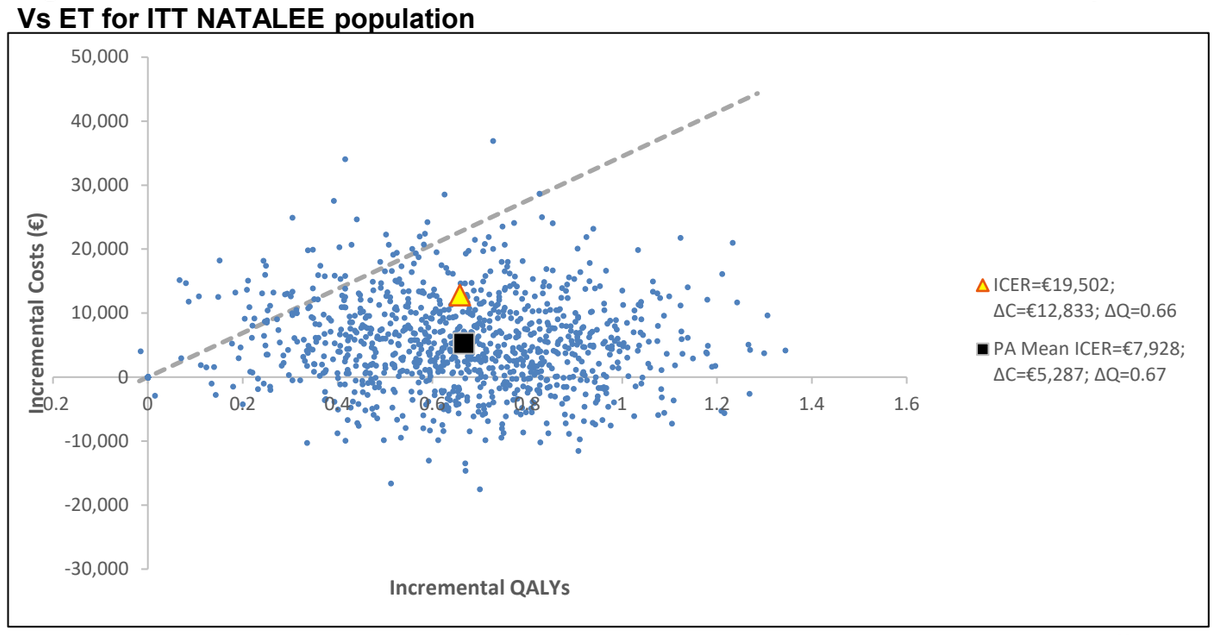


Abbreviations: ET: endocrine therapy; H: high; ICER: incremental cost effectiveness ratio; iDFS: invasive disease-free survival; L: low; PPS: post-progression survival

Probabilistic Sensitivity Analyses (PSA)

- The probabilistic base case was estimated with 1,000 bootstrapped Monte Carlo simulations of the parametric survival distributions estimated based on NATALEE clinical data.
- The estimated differences in QALYs and total discounted lifetime costs between ribociclib plus ET and ET monotherapy were also similar to those in the deterministic results in the base case. The probabilistic ICER of ribociclib plus ET versus ET monotherapy was €7,928 per QALY gained, which is lower than that estimated in the deterministic analysis (€19,502)

Figure 3. Probabilistic Simulations in the Cost-Effectiveness Plane for Ribociclib plus ET Vs ET for ITT NATALEE population



- In the MonarchE-eligible subgroup, ribociclib plus ET dominated abemaciclib plus ET, offering comparable health outcomes at a lower overall cost.
- According on PSA results, ribociclib plus ET was more cost-effective than abemaciclib plus ET across a range of willingness-to-pay (WTP) thresholds in MonarchE eligible population.
- PSA analysis confirmed the dominance of ribociclib plus ET, with the mean incremental cost favoring ribociclib plus ET (ΔC = -€9,570).

Disclosures

This study was funded by Novartis Hellas. All authors contributed to interpretation of the results, preparation, review and approval of the final poster. VA is employee of Novartis Hellas. MK is an employee of IQVIA Hellas, which was a paid consultant to Novartis in connection with the development of this study. ML was an employee of IQVIA Hellas at the time of this study was conducted.

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FA-11546145