Poster **410P**

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# Breast Cancer Lighthouse non-interventional hybrid real-world study: molecular characterization and 2-year effectiveness data

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## KEY FINDINGS & CONCLUSIONS

- This BC Lighthouse study interim analysis evaluated molecular characterization of disease and effectiveness at 24 months;
- During the 24-months follow-up, there is a 57% probability for a patient to require dose adjustment (mainly a single dose adjustment) and 60% of treatment interruption;
- In this 24-months of follow-up analysis roughly 16% and 32% had complete and partial responses, respectively;
- In line with the clinical trial outcomes, the median PFS was 22.6 months in this real-world study;
- Regarding mutational characterization, gBRCA mutations was reported in 21% of the BRCA tested patients. PIK3CA mutation was reported 30% of PIK3CA tested patients;
  - PIK3CA mutational testing was performed throughout the treatment course
- The PFS estimates for patients according to mutational gBRCA and PIK3CA status and molecular features as luminal status, ki-67 and HER2 classification (0 vs low) did not show a statistical difference.

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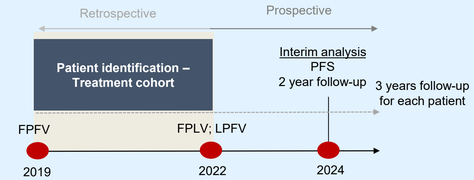
## INTRODUCTION

- Breast Cancer (BC) is the most common cancer in women, with an estimated 464,000 new cases diagnosed in 2012 in Europe[1]. Published data indicate that 5-10% of women presenting with BC have advanced disease with distant metastases, and it is estimated that around 20-30% of those presenting with early or localized breast cancer will develop ABC in the 10 years following diagnosis[2];
- Germline BC gene mutations (BRCA 1/2) have been detected in approximately 10% of HER2-negative BC cases[3]. On the other hand, PIK3CA is mutated in approximately 40% HR+/HER2- BC[4].
- For HR+/HER2- advanced/metastatic BC (ABC) patients, the European Society for Medical Oncology (ESMO) guidelines recommend the initiation of therapy with endocrine therapy in monotherapy or cyclin-dependent kinase 4/6 inhibitor (CDK4/6i)-based regimens. After the first line therapy, the choice of second line therapy regimen depends on the previous therapies used and the recommended options including endocrine therapy in monotherapy and/or targeted therapies[2];
- CDK4/6i treatment in ABC have shown benefit in progression-free survival (PFS) and on another clinical endpoints in landmark clinical trials. This study aims to comprehend real-world use of ribociclib in the Portuguese population and corresponding effectiveness and safety as well as the mutation pattern across the study population.

## METHODS

- Non-interventional hybrid study of a Portuguese cohort of adult women with HR+/HER2- advanced or metastatic BC that initiated treatment with ribociclib from 1st January 2019 to 31st December 2021, with retrospective and prospective secondary data collection from electronic medical records (EMR) of the participant hospitals. Included patients are followed-up through 3 years;
- In this present analysis, ribociclib treatment patterns (including prescribed dose), PFS at 2-year follow-up after ribociclib initiation, mutational analysis and others secondary endpoints are reported. Data was collected between January 2019 and January 2024, with analysis cut-off date of April 10, 2024 (**figure 1**). Confidence intervals and survival analyses were performed using R® software.

**Figure 1. Study design**




FPFV, first patient first visit; FPLV, first patient last visit; LPFV, last patient first visit

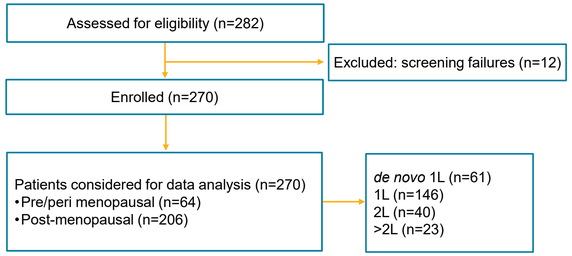
## RESULTS

- The present interim analysis details the ongoing observation of patients with ABC undergoing ribociclib treatment at study enrolment over a 24-month follow-up period (median of 23.9 months). The main outcomes of interest for this analysis were the molecular characterization of disease and effectiveness during the second year of follow-up.

### Patient characteristics

- A total of 282 patients diagnosed with advanced or metastatic BC were considered eligible for the study (**figure 2**). Of these, 12 were excluded due to a screening failure and 270 were included in the study.
- The study enrolled 270 patients at baseline. Of these, 84 died and 4 dropped out during the 24-month period.

**Figure 2. CONSORT flow diagram of the study population**




- Metastatic number of sites was evenly distributed across the different categories. However, with regards to metastasis location bone (197, 73.0%), lung (83, 30.7%), liver (74, 27.4%) and lymph nodes (113, 41.9%) were the most frequent. Of note that ribociclib was used by 136 (50.4%) patients with visceral metastasis;
- Majority of patients were classified as Luminal B-like (183, 67.8%) and with tumor G2 grade classification (168, 62.2%) or G3 (n= 57, 21.1%);

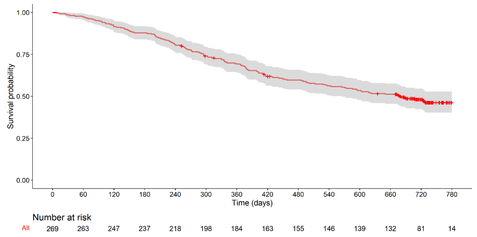
### Ribociclib treatment pattern

- At 24-month follow-up ribociclib treatment was discontinued by 155 of the 269 patients under risk, mainly due to disease progression. This leads to a median treatment duration of 17 months.
- During the two year's follow-up, there is a 57% probability for a patient to require a dose adjustment, mainly a single dose reduction (median to 1st dose adjustment of 12 months). AEs were the most common reason for dose adjustments.
- During this period, 133 patients required treatment interruption, corresponding to 60% likelihood of a patient to undergo a treatment interruption (median to 1st treatment interruption of 15.4 months). AEs were the most common reason for treatment interruption.

### Efficacy and safety

- Over the 24-month follow-up period, there were 140 documented instances of disease progression or death, among the 269 patients at risk. The median treatment duration until progression or death was 22.6 months (**figure 3**).
- Upon 24-month follow-up time, there was 20 (7.4%) patients that achieved complete response, 43 (15.9%) patients that had partial response and 85 (31.5%) that has stable disease. This translates into an objective response rate (ORR) of 23.3% and a clinical benefit rate (CBR) of 54.8%.
- The most prevalent AE was neutropenia, occurring 393 times (47.1%) and experienced by 150 patients (55.6%).

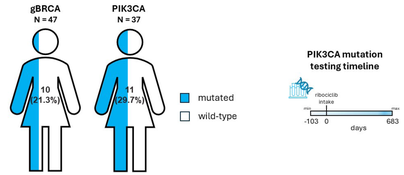
**Figure 3. Kaplan-Meier curve for time from ribociclib initiation until disease progression or death.**




### Mutation and biomarker analysis

- Overall, 47 (17.5%) patients were tested for gBRCA (mutated: 10, 21.3%) and 37 (13.7%) for PIK3CA (mutated: 11, 29.7%) (**figure 4**). Twenty-one patients (7.8%) were tested for both genes.

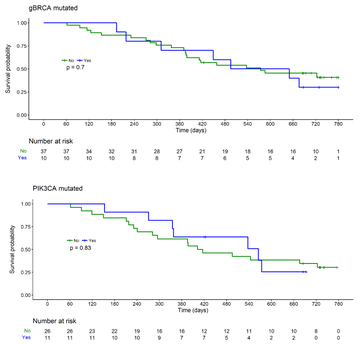
**Figure 4. Mutational profile of the patients tested for gBRCA and PIK3CA.**




* The time to PIK3CA mutation testing ranged from 103 days before ribociclib initiation to 683 days post-treatment start, reflecting the ongoing monitoring of molecular changes throughout the treatment course

- The mutational profile based on luminal, HER2 and ki-67 classification/status showed that a higher request of mutation testing was performed in luminal B and ki-67≥20% patients when compared to luminal A and ki-67<20%, respectively. No difference was observed for HER2 classification.
- Although smaller size, the PFS estimates for patients according to gBRCA and PIK3CA status did not show a statistical difference (**figure 5**). The same is true for luminal status (A vs B), ki-67 (<20% vs ≥20%) and HER2 classification (0 vs low).

**Figure 5. Kaplan-Meier curve for the time from ribociclib start until disease progression or death per gBRCA and PIK3CA mutation status. Yes= Mutated; No= Wildtype.**





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## Disclosures

Daniel Brás and Marco Domingues are Novartis Farma employees