Updated analyses from the retrospective rAMBER study exploring abemaciclib monotherapy after prior CDK4/6 inhibitor progression in metastatic hormone-receptor positive breast cancer

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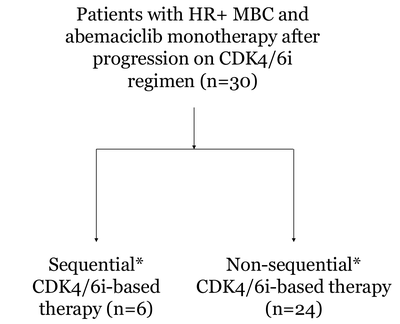
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01. Introduction

- Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) have become the standard of care for patients with advanced HR+/HER2- breast cancer.
- There remains uncertainty regarding the efficacy of CDK4/6i re-introduction after progression on CDK4/6i.
- We provide updated data and analysis from rAMBER: retrospective multi-center, biomarker study to evaluate efficacy of abemaciclib monotherapy beyond first line CDK4/6 inhibition in ER+ breast cancer.

02. Methods

- Collected retrospective patient data at 4 academic cancer centers (Massachusetts General Hospital, Barnes-Jewish Hospital, University of Pittsburgh Medical Center, Moffitt Cancer Center).
- Identified patients with metastatic HR+/HER2- breast cancer with disease progression on CDK4/6i-based therapy who received *abemaciclib monotherapy*.



Data (collected via IRB-approved protocols):
- Demographics and clinical outcomes
- Serial RECIST measurements from imaging studies
- Solid tumor and cfDNA for targeted sequencing

* Sequential signifies no intervening treatments between prior CDK4/6i therapy and abemaciclib monotherapy

03. Clinical and radiographic outcomes

- 23/30 patients remained on abemaciclib until either disease progression or death, while the remaining 7 discontinued treatment due to adverse side effects (Figure 1).
- Median duration of abemaciclib treatment was 4.0 months (95% CI: 2.8-13.9 months) after progression on palbociclib-based therapy (Figure 2a). Patients received a median of two intervening lines of therapy between palbociclib and abemaciclib.

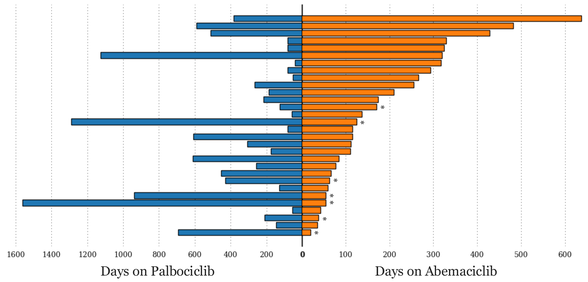


Figure 1. Duration of palbociclib regimen (blue) and abemaciclib regimen (orange) per patient in days. Bars with * represent patients who did not tolerate abemaciclib due to toxicity.

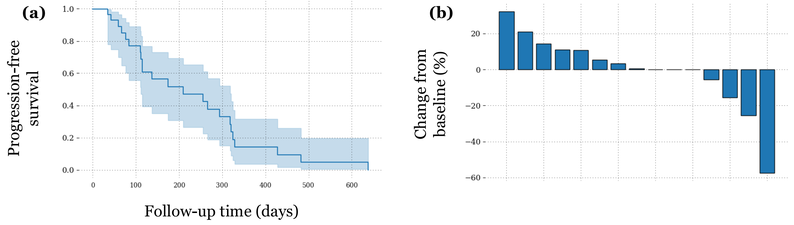


Figure 2. (a) Median duration of abemaciclib treatment was 4.0 months (95% CI: 2.8-13.9 months) after progression on palbociclib-based therapy. (b) Best radiographic response for target lesions per patient (only includes MGH cohort): 1 patient with partial response, 7 with stable disease, and 8 with progressive disease.

04. Genomic exploration

- Figure 3 summarizes results from genomic assays on 23 biopsies.
- Each biopsy is assigned a phenotype (sensitive, acquired resistance, or intrinsic resistance) based on best clinical response and duration of response in relation to biopsy timing.
- *RB1* alterations are associated with acquired/intrinsic resistance while *ESR1* alterations can be found across all biopsy phenotypes.

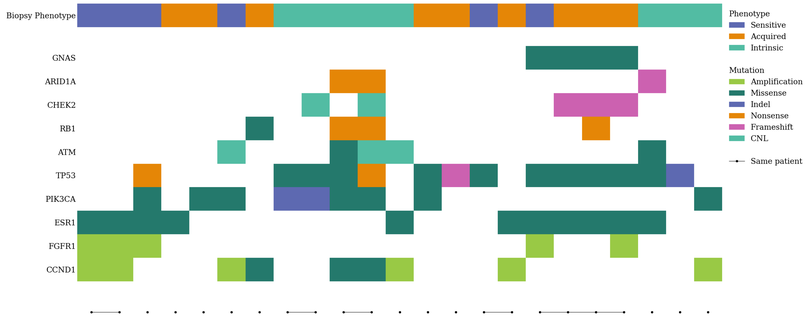


Figure 3. CoMut plot visualizes the genetic alterations found in the rAMBER cohort. Only top 10 most commonly altered genes are shown.

05. Conclusions

- One third of patients derived benefit from abemaciclib monotherapy, tolerating the regimen for > 180 days, despite progression on prior palbociclib and endocrine therapies.
- Preliminary genetic analyses revealed enrichment in RB1 alterations in patients with rapid disease progression.
- rAMBER is the first to evaluate the effectiveness of abemaciclib monotherapy after progression on CDK4/6i, offering new perspectives on the role of sequential CDK4/6 therapies.

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