Efficacy and activity of treatments after progression from palbociclib plus endocrine therapy in patients with HR+/HER2- metastatic breast cancer: a prospective, real-world study

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Main baseline characteristics whole cohort (N = 79)

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<tr>
<th>Median age, years (range)</th>
<th>≤ 65</th>
<th>&gt; 65</th>
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<td>54.3 (33-78)</td>
<td>50 (47-76)</td>
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ECOG PS
- 0: 55 (69.6%)
- 1: 21 (26.5%)
- 2: 3 (3.7%)

Menopausal status
- Pre: 34 (43.0%)
- Post: 45 (56.9%)

Histology
- Ductal: 58 (73.4%)
- Lobular: 21 (26.5%)

Receptor status
- ER >10: 79 (100%)
- PgR >20: 56 (71.9%)
- Ki67 <20: 55 (69.6%)
- >20: 24 (30.4%)

Grade
- G1/G2: 65 (82.3%)
- G3: 14 (17.7%)

Visceral metastases
- No: 41 (51.9%)
- Yes: 38 (48.1%)

Adjuvant CHT regimen
- Anthracyclines: 26 (55.3%)
- Antracyclines + taxane: 16 (20.2%)
- CMF: 5 (10.7%)

Adjuvant ET type
- Anastrozole: 31 (39.2%)
- Letrozole: 12 (15.2%)
- Exemestane: 4 (2.5%)
- Tamoxifen: 12 (15.2%)
- Tamoxifen + LH-RH: 15 (19.0%)
- Missing: 7 (9.1%)

Endocrine resistance
- Primary: 11 (13.9%)
- Secondary: 56 (70.9%)
- De novo metastatic disease: 12 (15.2%)

Line for Palbociclib therapy
- 1st: 22 (27.8%)
- ≥ 2: 57 (72.2%)

Concomitant ET with Palbociclib
- Aromatase Inhibitors: 22 (27.8%)
- Fulvestrant: 57 (72.2%)

Background
- The association of ET and CDK 4/6 inhibitors (CDK 4/6) is the gold standard of treatment in women with HR+/HER2- MBC
- The optimal therapeutic strategy after CDK 4/6 progression is still a matter of debate
- Our prospective study aimed to evaluate the benefit of the different treatments adopted in a real-world context

Patients & Methods
- From May 2017 to October 2021, 78 pre- and postmenopausal patients were enrolled; 56 were evaluable for the final analysis
- Either ET or CT were prescribed considering: 1) site/burden of disease; 2) mPFS1 (< vs ≥ 4 months); 3) patient’s compliance/preferences
- Primary aim: median PFS (PFS2)
- Secondary aims: analysis of the determinants of physician’s choice, clinical benefit rate (CBR), impact of neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR) and body mass index (BMI) on PFS2

Results
- In the whole population mPFS1 was 17.5 months; mPFS2 was 5 months in the overall cohort (95% CI = 4-48 months) with a significant difference between ET and CT (10 vs 5 months, p=0.035); CBR was 50% and 55.2%, in ET and CT cohort, respectively
- At multivariate analysis CT prescription was associated to a higher visceral burden and a shorter mPFS1. Elevated NLR and PLR were correlated with worse PFS2 in both treatment groups, while no impact of MLR and BMI was observed

Conclusions
- In our real life experience, treatments beyond ET plus Palbociclib failure provided limited but comparable clinical benefit
- The physician’s choice was clearly driven by disease’s burden
- The inflammatory status seems to have a detrimental effect on median PFS2

Characteristics of patients who started therapy after PD on palbociclib/ET (N = 56)

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<td>50.7 (33-75)</td>
<td>59 (47-76)</td>
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ECOG PS
- 0: 35 (62.5%)
- 1: 21 (37.5%)

Menopausal status
- Pre: 24 (42.8%)
- Post: 32 (57.1%)

Histology
- Ductal: 36 (64.2%)
- Lobular: 20 (35.7%)

Receptor status
- ER >10: 56 (100%)
- PgR >20: 15 (26.7%)
- PgR >20: 41 (73.2%)

Ki67
- <20: 39 (69.6%)
- >20: 17 (30.3%)

Grade
- G1/G2: 43 (76.7%)
- G3: 13 (23.2%)

Visceral metastases
- No: 35 (62.5%)
- Yes: 21 (37.5%)

Adjuvant CHT regimen
- Anastrozole: 22 (39.2%)
- Letrozole: 17 (30.3%)
- Exemestane: 13 (23.2%)
- Tamoxifen: 10 (17.8%)
- Tamoxifen + LH-RH: 12 (21.4%)
- Missing: 4 (7.1%)

Adjuvant ET type
- Anastrozole: 17 (30.3%)
- Letrozole: 13 (23.2%)
- Exemestane: 10 (17.8%)
- Tamoxifen: 12 (21.4%)
- Missing: 4 (7.1%)

Endocrine resistance
- Primary: 11 (19.6%)
- Secondary: 38 (67.8%)
- De novo metastatic disease: 7 (12.5%)

Line for Palbociclib therapy
- 1st: 14 (25.0%)
- ≥ 2: 42 (75.0%)

Concomitant ET with Palbociclib
- Aromatase Inhibitors: 24 (42.8%)
- Fulvestrant: 32 (57.1%)