Methods: ER+, HER-2- mBC patient candidates for palbociclib as first-line treatment were enrolled in this retrospective observational study. Patients were defined as "no concomitant PPIs" if no PPI were administered during palbociclib, and as "concomitant PPIs" if the administration of PPIs covered the entire or not less than 2/3 of treatment with palbociclib. All clinical interventions were made according to clinical practice.

Results: A total of 112 patients were enrolled; 56 belonged to "no concomitant PPIs" during palbociclib treatment and 56 to the "concomitant PPIs" group. Seventy-one patients were endocrine sensitive (ES) and were administered palbociclib + letrozole and 41 were endocrine resistant (ER) and were treated with palbociclib + fulvestrant. The most prescribed PPI was lansoprazol. Patients were stratified according to PFS, showing that patients taking PPIs had a shorter PFS compared to patients assuming palbociclib + hormone-therapy alone (14 vs 38 months, $p<0.0001$). Multivariate analysis confirmed the use of concomitant PPIs as the only independent predictive factor for shorter PFS ($p=0.0002$). PFS was significantly longer in ES mBC with no concomitant PPIs compared to patients taking PPIs or ER patients with and without PPIs ($p<0.0001$). No correlation with adverse events was found considering $G>2$ hematological toxicities.

Conclusions: The present study demonstrates that concomitant use of PPIs in mBC patients treated with palbociclib has a detrimental effect on PFS. Therefore, it is recommended to prescribe PPI with caution in these patients, or administering H2-antagonists or PPI for very short periods.

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240P A real-world data analysis: The first United Kingdom experience of cyclin-dependent kinase 4/6 inhibitor in advanced breast cancer in the National Health Service within an access program

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Background: An aromatase inhibitor in combination with a cyclin-dependent kinase 4 and 6 inhibitor (CDKi 4/6) is now the standard of care for HR+/HER2-, locally advanced (LA) and metastatic breast cancer (MBC). Palbociclib was the first CDKi 4/6 generally accessible within the National Health Service (NHS) via the Palbociclib Patient Programme (PPP) with 848 patients initiating palbociclib treatment on the PPP. This study examined the use, effectiveness, and toxicity of palbociclib within the PPP.

Methods: Patients with LA/MBC treated at 8 centres within the PPP between April and December 2017 were eligible. Presented here are the initial data of patients treated in the 1st line setting (1L). Clinical records were reviewed with clinico-pathological, treatment, outcomes, and safety data.

Results: Of the 191 patients recruited, 140 were 1L: median age (interquartile range) 57.6 years (48.6 - 68.9); 50% (68/136) pre/peri-menopausal; 29% (n=40) presented with de novo LA/MBC; 33% (46/138) had visceral and 67% (92/138) non-visceral disease, 47% (65/138) bone-only. Observation period (OP) was 24 months from palbociclib initiation. At the end of OP, complete or partial response and stable disease were recorded as best response in 91% (127), progression in 6% (9) and 'unknown' response 3% (4); median progression-free survival (mPFS) was 22.5 months, median overall survival (mOS) not reached (NR), mPFS and mOS NR for de novo patients, nor those who relapsed >12 months from end of adjuvant treatment (n=41). At the end of OP, 51% (71) remained on treatment and 49% (n=69) discontinued (80% [55/69] due to disease progression); 43% (n=60) had ≥1 treatment interruptions and dose reductions were: none 57% (80) and >1 reduction 43% (60) (includes: 20% [28] <3 months, 11% [15] 3-6 months and 12% [17] ≥6 months).

Conclusions: These data from the first NHS patients treated with CDK4/6i outside of a clinical trial indicate the real-world effectiveness and tolerability of palbociclib and complements the pivotal studies. Patient access schemes may bridge the gap between regulatory approval and NHS funding for new medicines and can facilitate collection of data to evaluate outcomes in routine practice.

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241P Abemaciclib plus fulvestrant in participants with HR+/HER2- advanced breast cancer: A pooled analysis of the endocrine therapy naïve (EN) participants in MONARCH 2

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Background: MONARCH 2 (M2) demonstrated that the addition of continuously-dosed abemaciclib to fulvestrant significantly improved progression-free survival (PFS) and overall survival (OS) compared to placebo plus fulvestrant in women with HR+, HER2- advanced breast cancer (ABC) who had progressed on endocrine therapy (ET). Here we present the Objective Response Rate (ORR) from endocrine-naïve (EN) participants enrolled in MONARCH 2.

Methods: A small cohort of EN participants, with measurable disease at baseline, were initially enrolled in the M2 main study [excluded from the intent-to-treat (ITT) population] (N=20). Subsequently, 90 additional participants were enrolled under the EN addendum. The analysis population consist of a pooled EN cohort (N = 110). All participants were scheduled to receive abemaciclib (150mg or 200 mg Q12H) plus fulvestrant (500 mg, per label). Participants were not allowed to have had prior ET in any setting or prior chemotherapy in the metastatic setting. The primary endpoint was investigator-assessed confirmed ORR. The secondary endpoints were investigator-assessed PFS, duration of response (DoR), disease control rate (DCR), clinical benefit rate (CBR), and safety and tolerability.

Results: In the pooled EN cohort, confirmed ORR was 59.1% (95% CI 49.9-68.3). Median follow-up was 9.8 (0.03-73.05) months. PFS and DoR data are not mature at this time. No new safety signals were reported in the pooled EN cohort, and the safety profile was consistent with the previously reported MONARCH 2 population.

Conclusions: The primary analysis of confirmed ORR compares favorably with previously reported ORR for fulvestrant monotherapy in participants with a similar disease state. PFS and DoR data are not yet mature. The safety profile is similar to that previously reported in the primary MONARCH 2 main study.

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