**Title:** Hormonal therapy combined with Ribociclib for patients with advanced ER positive breast cancer: Real World Data

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**Background:** CDK4/6 inhibitors, such as ribociclib, are recommended in combination with hormonal therapy to treat advanced or metastatic hormone receptor-positive, HER2-negative breast cancer. The objective of this study is to evaluate the tolerance and cardiac toxicity and therapeutic outcome of ribociclib in patients treated at one institution. **Methods:** Patients who received 2 or more cycles of ribociclib between December 2018 and March 2022 and were included. Rates of dose reduction of ribociclib were used as surrogate marker for intolerance and were compared to those reported in land-mark trials. QTc changes and cardiac adverse events (AEs) were also collected. **Results:** Sixty eight female patients were included. Ribociclib was administered in the first-, second-, third-, and fourth-line palliative hormonal therapy settings in 29 (42.6%), 26 (38.2%), 12 (17.6%) and 1 (1.5%) patients respectively and 17/68 (25%) received prior 1-4 palliative chemotherapy lines. Ribociclib was combined with letrozole in 42 (61.8%) and with fulvestrant in 26 (38.2%) patients. QTc interval was ≤ 480 msec in all patients prior to treatment and 19 (27.9%) patients had preexisting cardio vascular (non-electro-conductive) risks such as diabetes and hypertension. AEs related dose reduction was reported in 30 (44%) patients [Neutropenia 16/68 (23.5%), QTc prolongation 4/68 (5.8%), other cardiac concerns 2/68 (3%), abnormal liver function tests 3/68 (4.4%), abdominal pain 3/68 (4.4%) and not documented 2/68 (3%)]. Ribociclib was permanently discontinued in 42/68 (61.8%) patients [Disease progression 33/68 (48.5%) and AEs 9 (13.2%)]. AEs related discontinuation was due to QTc prolongation 2/68 (3%), other cardiac events or concerns 3/68 (4.4%), Neutropenia 2/68 (2.9%), COVID then patient refusal 1/68 (1.5%), patient inability to commit to ECG monitoring 1/68 (1.5%).

Objective response was evaluable in 61 patients [CR: 3 (4.9%), PR: 7 (11.5%), SD: 37 (60.7%) and PD: 14 (23%)]. The median progression free survival was 18 months (95% CI: 11.7-24.3). The median overall survival was not reached and the 84% orf patients were alive at 3 years.

**Conclusions:** Although objective response rates were modest in this mixed cohort of heavily pretreated patients, ribociclib combined with letrozole or fulvestrant has shown robust progression free and overall survival in real life practice. Toxicity related treatment discontinuation rate is higher than that reported in clinical trials with stringent inclusion criteria. Ribociclib associated cardiac toxicity require careful monitoring.

| **Safety Results** | | |
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|  | **Dose Reductions** | **Discontinuation due to adverse events** |
| This Study n=31 | 30 (44%) | 9 (13.2%) |
| MONALEESA-2 n=334 | 180 (53.9%) | 25 (7.5%) |
| MONALESSA-3 n=484 | 183 (37.9%) | 41 (8.5%) |
| MONALESSA-7 n=335 | 117 (34.9%) | 12 (3.6%) |