Clinical Implications of Body Mass Index and Weight Changes in Metastatic Breast Cancer Patients Treated with Abemaciclib and Endocrine Therapy: a Combined Individual-Patient-Level Data Analysis of MONARCH 2 and MONARCH 3 Trials

Maria Alice Franzoi1, Daniel Eiger2, Lieveke Ameye1, Noam Ponté4, Claudia De Angelis1, Rafael Caparica1, Mariana Brandão6, Natale Kotecki7, Marianne Paesmans1, Matteo Lambertini1, Serena Di Cosimo1, Christine Desmedt1, Ahmad Awaad1, Martine Picart-Gebhart2, Evandro de Azambuja1

1Institut Jules Bordet, Brussels, Belgium; 2AC Camargo Cancer Center, São Paulo, Brazil; 3University of Genova and IRCCS Ospedale Policlinico San Martino, Genova, Italy; 4Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Italy; 5KU Leuven, Leuven, Belgium

Background

• There is limited data regarding the role of overweight/obesity in advanced breast cancer as previous studies focused mainly on the early setting.

• CDK 4/6 inhibitors combined with endocrine therapy (ET) are considered the standard of care for 1st or 2nd line treatment of hormone receptor (HR)-positive/HER2-negative metastatic breast cancer.

• Besides cell cycle regulation, CDK 4 and 6 are involved in important metabolic processes such as adipogenesis, gluconeogenesis and muscular metabolism.

• We analyzed the impact of body mass index (BMI) on progression-free survival (PFS) response rate (RR) and incidence of adverse events in patients receiving abemaciclib + ET vs. placebo + ET.

Methods & Objectives

• This was a post-hoc, pooled analysis of individual-patient-level data from the MONARCH 2 and 3 trials.

• Patients were classified according to BMI into underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²) and obese (>30 kg/m²) and divided into two treatment groups: abemaciclib + ET vs. placebo + ET.

• Primary end-point: To evaluate the association between BMI and PFS in each treatment group.

• Secondary endpoints: to analyze RR and the incidence of adverse events according to BMI as well as weight change (≥4% from baseline) during treatment. Impact of concomitant use of metformin and or statins in clinical outcomes.

• Statistical analyses: All PFS endpoint was assessed with Kaplan-Meier curves and log-rank test. Cox’s proportional hazard model was used to calculate hazard ratios and 95% confidence interval (CI). Multivariate analysis was performed adjusting for age, ECOG, metastatic site, prior ET, trial enrolled, menopausal status and progesterone receptor (PgR) positivity.

Results

• 1138 patients were included (757 in the abemaciclib + ET arm and 381 placebo + ET).

• 54% of the patients were overweight and obese and the prevalence varied significantly according to ethnicity, geographic region, age, comorbidities, menopausal and performance status.

• Patients with normal BMI presented higher ORR in the abemaciclib + ET arm compared to placebo + ET (Table 1).

• There was no difference in RR between BMI categories in both arms (Fig. 1), although obese patients presented a lower RR compared to patients with abemaciclib + ET compared to normal weight patients (Fig. 2).

• Obese patients experienced less neutropenia when treated with abemaciclib + ET (Box 1). Weight loss was 3 times more frequent in the abemaciclib + ET group and it was not related to treatment (Table 2).

• Concomitant use of metformin or statins did not impact clinical outcomes in none of the treatment groups.

Table 1: Response rates according to BMI

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Treatment</th>
<th>RR (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>abemaciclib + ET</td>
<td>placebo + ET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (BMI&lt;25 kg/m²)</td>
<td>410 (60.6%)</td>
<td>426 (63.1%)</td>
<td>0.76 (0.59-0.99)</td>
<td>0.042</td>
</tr>
<tr>
<td>Overweight (BMI 25–29.9 kg/m²)</td>
<td>221 (71.3%)</td>
<td>224 (72.4%)</td>
<td>0.99 (0.78-1.27)</td>
<td>0.940</td>
</tr>
<tr>
<td>Obese (BMI ≥30 kg/m²)</td>
<td>37 (57.1%)</td>
<td>42 (60.5%)</td>
<td>0.94 (0.61-1.46)</td>
<td>0.763</td>
</tr>
</tbody>
</table>

Table 2: Weight changes during therapy in both treatment groups

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weight change compared to baseline (months)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>abemaciclib + ET</td>
<td>-0.80 (2.08-5.01)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>placebo + ET</td>
<td>3.23 (2.04-7.23)</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Fig. 1: PFS according to BMI in both treatment groups

Fig. 2: PFS in normal weight patients receiving Abemaciclib + ET vs. Placebo + ET. Abemaciclib patients had a longer PFS (21.9 vs. 10.8 months), hazard ratio 0.48 (95% CI, 0.38-0.61), p-value <0.001.

Fig. 3: PFS in obese patients receiving Abemaciclib + ET vs. Placebo + ET. Abemaciclib patients had a longer PPS (20.2 vs. 11.6 months), hazard ratio 0.70 (95% CI, 0.50-0.97), p-value 0.03. Interaction test (BMI and PPS) p=0.07.

Conclusions

• Overweight/obesity is quite prevalent among patients with metastatic breast cancer (54.3% in this analysis).

• Adding abemaciclib to ET increases PFS regardless of BMI, showing that overweight/obese patients also benefit from this regimen.

• Obese patients presented a lower magnitude of benefit, inferior response rates and lower neutropenia rates when treated with abemaciclib + ET when compared to normal weight patients, questioning optimal dose-intensity in this patient population.

• Patients under treatment with abemaciclib + ET presented statistically more loss of weight at 6, 12 and 18 months when compared to ET alone, which might be related to a possible effect of abemaciclib on reducing fat mass as previously described in mouse models.

Box 1: Adverse events in the abemaciclib + ET group. Overweight/obese patients presented less any grade neutropenia (51.0 vs. 40.4% p=0.004) and grade 3 neutropenia (29.3% vs. 21.7% p=0.02) when compared to normal weight patients. There were no statistically differences regarding diarrhea.

Disclosures

References