Factors associated with first line chemotherapy use in patients with hormone receptor positive, HER2 negative metastatic breast cancer – data from the PRAEGEN breast cancer registry

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BACKGROUND
For breast cancer patients with metastases which are not HER2 positive, endocrine therapies are considered as first line treatment, even for patients that are considered for receiving chemotherapeutic treatment. In Germany as of 2014 only 4% of patients with hormone receptor positive, HER2 negative metastatic breast cancer received chemotherapy. CIBA-endocrine treatment (CDK4/6 inhibitors) recently became available in Germany which might change the treatment algorithm. The analysis used data from a registry for metastatic breast cancer focus. Patients are first line treated with endocrine receptor positive, HER2 negative (trastuzumab) breast cancer.

Aims of this analysis was the description of the patients that are associated with use of chemotherapy vs. endocrine (endocrine) based treatment. A further aim was the description of the distribution of chemotherapy vs. endocrine therapy over the last years as their effect on time to chemotherapy induction is evaluated.

STUDY DESIGN AND METHODS
The PRAEGEN data set (NCBZ-021384) is considered as a prospective diagnostic translational and multicentric registry with a central documentation of patient and tumor characteristics and a central biobank archive for prospective molecular analysis. The study network aims at registering 10,000 breast cancer patients with advanced, incurable, metastatic disease.

This analysis was restricted to first line metastatic patients who were hormone receptor (HR) positive and HER2 negative.

Data collection
Clinical data were collected by trained and dedicated staff at the 22 participating institutions of the PRAEGEN study (Table 1). Patients were monitored using automated plausibility checks and through regular clinical re-evaluations.

Statistical analysis
Associations between various patient and tumor characteristics and first line therapy (endocrine therapy vs. anthracycline therapy) were analyzed using a multiple logistic regression model. Overall survival of patients with chemotherapy vs. endocrine therapy at first line was compared using a multiple Cox survival model with the same predictor variables as above. Relative risks and 95% confidence intervals were provided to estimate the effect size.

RESULTS
Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Endocrine (N=452)</th>
<th>Chemotherapy (N=88)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year)</td>
<td>50.3(78)</td>
<td>43.6(106)</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI(kg/m2)</td>
<td>25.7(6)</td>
<td>26.7(7)</td>
<td>0.17</td>
</tr>
<tr>
<td>ECOG</td>
<td>0.9(1)</td>
<td>1.6(4)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

A detailed distribution of the four therapy options is shown in Figure 1. Chemotherapy use already decreased before the availability of CIBA. After the availability of CIBA, chemotherapy use decreased further. However, it is evident, that most of the patients are recruited from the group of patients who previously were treated with anthracycline monotherapy. Table 1: Patient characteristics

Table 3: Cox regression model for overall survival

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year)</td>
<td>0.96 (0.94, 0.98)</td>
</tr>
<tr>
<td>BMI(kg/m2)</td>
<td>0.97 (0.95, 0.99)</td>
</tr>
<tr>
<td>ECOG</td>
<td>0.88 (0.78, 0.99)</td>
</tr>
</tbody>
</table>

CONCLUSION
The usage of chemotherapy can be predicted with age, metastatic pattern and ECOG. Furthermore, chemotherapy use has decreased over time inducing the use of chemotherapy as 1st line therapy for HR+HRL2-patients. CIBA/anthracyclines are used frequently as 1st line metastatic setting since its introduction into the German market.

Patients treated with chemotherapy as 1st line metastatic setting have a rather unfavourable survival compared to patients treated with endocrine therapy, which is likely to be treated with another chemotherapy.

ACKNOWLEDGEMENT
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Table 4: Cox regression model for first line chemotherapy use

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year)</td>
<td>0.99 (0.98, 1.00)</td>
</tr>
<tr>
<td>BMI(kg/m2)</td>
<td>0.97 (0.95, 1.00)</td>
</tr>
<tr>
<td>ECOG</td>
<td>0.99 (0.97, 1.00)</td>
</tr>
</tbody>
</table>

Figure 1: Chemotherapy use already decreased before the availability of CIBA. After the availability of CIBA, chemotherapy use decreased further. However, it is evident, that most of the patients are recruited from the group of patients who previously were treated with anthracycline monotherapy. Overall survival according to choice therapy

A multivariate Cox regression model for first line therapy chemotherapy vs. HR positive showed a statistically significant effect on overall survival. Especially patients with brain metastases and patients with a high grading of the primary tumor had an unfavourable prognosis concerning overall survival. Chemotherapy use was also associated with an unfavourable prognosis (Hazard ratio 3.6; 95% CI; 1.19, 11.9). Table 4: Cox regression model for first line chemotherapy use

Figure 2: Chemotherapy use already decreased before the availability of CIBA. After the availability of CIBA, chemotherapy use decreased further. However, it is evident, that most of the patients are recruited from the group of patients who previously were treated with anthracycline monotherapy. Overall survival according to choice therapy

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Figure 3: Distribution of first line treatment of HR+HRL2 patients over time

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