Prevalence and trends in 1L treatment

Study Population

- We included 5,259 HR+/HER2- patients diagnosed with mBC between 1/1/2015 and 10/31/2018 (dataset cutoff 12/30/2019) who were ≥18 years at diagnosis and received ≥1L treatment in the Flatiron Health EHR network.

Prevalence and Trends in 1L treatment

- 94% patients received ET + CDK4/6i, 30% received monotherapy (mono), and 9% received chemotherapy without ET. 10% received other regimens (mono) ET + chemotherapy or chemotherapy alone.
- Patients were ≥18 years at diagnosis and received ≥1L treatment in the Flatiron Health EHR network.

Predictors of 1L treatment

- Patients were less likely to receive ET + CDK4/6i (vs. ET mono) if they were older or had higher ECOG PS, but more likely if they had metastases beyond bone (Figure 2).

Real-world predictors of first-line treatment and descriptive outcomes in patients with HR+/HER2- metastatic breast cancer in the US

Table 2. Characteristics by 1L treatment category for HR+/HER2- patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ET Mono</th>
<th>ET + CDK4/6i</th>
<th>Chemotherapy</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range)</td>
<td>63 (45-86)</td>
<td>67 (54-87)</td>
<td>61 (35-89)</td>
<td>70 (47-85)</td>
</tr>
<tr>
<td>ECOG PS (closest to 2L)</td>
<td>0.96 (0.79-1.15)</td>
<td>0.86 (0.69-1.06)</td>
<td>1.00 (0.90-1.11)</td>
<td>0.97 (0.79-1.18)</td>
</tr>
<tr>
<td>ECOG PS (closest to diagnosis)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>ECOG PS (closest to 1L)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>OS (95% CI)</td>
<td>14.4 (12.7, 16.1)</td>
<td>14.1 (12.4, 15.8)</td>
<td>12.0 (10.2, 13.8)</td>
<td>14.9 (13.1, 16.7)</td>
</tr>
<tr>
<td>TTN (95% CI)</td>
<td>10.5 (9.5, 11.6)</td>
<td>10.2 (9.2, 11.3)</td>
<td>8.1 (7.0, 9.2)</td>
<td>11.3 (10.1, 12.5)</td>
</tr>
</tbody>
</table>

Table 3. Multivariable proportional hazards models estimating the HRs and 95% CI of 1L treatment with OS and TTN in HR+/HER2- mBC patients.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Model</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>ET Mono vs. Chemotherapy</td>
<td>1.38 (0.78, 2.47)</td>
<td>0.276</td>
</tr>
<tr>
<td></td>
<td>ET Mono vs. Other</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>TTN</td>
<td>ET Mono vs. Chemotherapy</td>
<td>0.67 (0.42, 1.07)</td>
<td>0.093</td>
</tr>
<tr>
<td></td>
<td>ET Mono vs. Other</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
</tbody>
</table>

Outcomes Analyses
- Median OS (Figure 3) and TTN (Figure 4) were shortest among patients receiving chemotherapy and longest in patients receiving ET + CDK4/6i. This held after adjusting for potential confounders in multivariable cox proportional hazards regression models (Table 3).

Figure 3. Overall survival by 1L treatment category.

Figure 4. Time to next treatment by 1L treatment category.

CONCLUSIONS

- ET + CDK4/6i is an increasingly common 1L treatment choice for patients with HR+/HER2-mBC and is displacing ET mono as the standard of care, particularly among patients who were younger and had better ECOG PS at mBC diagnosis. Patients receiving ET + CDK4/6i also had superior outcomes.
- Patients who received chemotherapy had inferior outcomes, consistent with expectations that these patients have a poorer prognosis at mBC diagnosis (Eshleman et al., 2017).
- These findings support the clinical benefit observed in published randomized clinical trials of ET vs. ET mono regimens (Turner et al., 2019).

REFERENCES

ACKNOWLEDGMENTS
- Genentech, Inc. sponsored this study and provided support for the preparation of this poster.

STUDY STRENGTHS
- EHR data from Flatiron Health, which is unique in its completeness and quality of key variables needed for research (e.g. death date with 87% sensitivity [Curts et al., 2018] biomarker data to determine mBC subtypes, and more) lend credibility to these findings.
- Data on recent patient follow-up (i.e. through July 2019) allowed us to examine trends and uptake of CDK4/6i, a newer therapeutic agent.

LIMITATIONS
- Because randomization is impossible in clinical practice, residual confounding may still be possible due to an influence of unmeasured factors (i.e. even after covariate adjustment).
- Despite high completeness of key variables, other important covariates such as ECOG PS are not well captured in EHRs; misclassification may occur due to documentation practices or interventions administered outside the clinics withinFlatiron network. This may further contribute to residual confounding or misclassification in our multivariable adjusted models.
- An algorithm was used to determine line of therapy, which may not be accurate due to the potential missing information in the EHR. For example, if 3L is received outside the Flatiron network, we may incorrectly assign it as 1L, as well.
- TTN is a proxy for PFS, but also captures changes in treatment for other than progression (e.g. toxicities, physician or patient preference, insurance coverage, etc.).
- For some regimens, small sample sizes limit precision and inferences.
- Results may not be generalizable to patients treated in US academic centers or ex-US centers.

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