Brain Metastases in Primary Ovarian Cancer: Real-world Data

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OBJECTIVES
• To assess whether BRCA wild-type patients have a decreased risk of developing brain metastases compared with BRCA-mutated patients.

METHODS
• This retrospective study included 40,115 OC patients diagnosed between January 1, 2011 and January 31, 2018 from the Flatiron Health database. Flatiron is a longitudinal, demographically and geographically diverse database derived from electronic health record data from over 265 cancer clinics and over 2 million active US cancer patients.
• The outcome of this study was the development of brain metases after the OC diagnosis.
• A time-to-event analysis was conducted to assess whether patients with a known BRCA status were more likely to develop brain metastases compared with patients with BRCA wild-type status.

RESULTS
• Of 40,115 OC patients, 2223 (4%) had BRCA testing and 2306 (5%) had BRCA status unknown or not tested (Table 1).
• Of the 2223 patients who underwent BRCA testing, 473 (21%) were BRCA-mut, 1679 (76%) were BRCA-wt, and 54 (2%) had unknown BRCA status.
• Overall, in this population, 46 (1%) patients developed brain metastases.
• Brain metastasis rate was significantly higher in OC patients with brain metastasis (38%) as compared to those without (21%).
• Patients who developed brain metastases were younger than patients without metastases at the time of OC diagnosis.

• The median overall survival after diagnosis of brain metastases was 7.16 months (95% CI 3.48, 15.42) (Figure 2). Survival after brain metastases diagnosis did not differ significantly by BRCA status (data not shown).
• Of the 473 BRCA-mut patients, 211 (45%) had a BRCA1 mutation, 151 (32%) had a BRCA2 mutation, and 7 (1%) had both mutated BRCA1 and BRCA2 (Figure 4).
• Of the 14 BRCA-wt patients who developed brain metastases in the study, 8 (47%) had BRCA1 mutation, 4 (25%) had BRCA2 mutation, and 2 (14%) had BRCA wild-type status (included in the 2 prior cohorts as well), and 2 (14%) had a germline variant that favors a polymorphism/BRCA not otherwise specified (Figure 5).

CONCLUSIONS
• OC patients with a BRCA mutation displayed a 4-fold increased risk of developing brain metastases than patients without a BRCA mutation.
• Despite being a rare complication of OC, the possibility of developing brain metastases should be considered in these patients, especially those with BRCA mutation.
• The availability of new therapeutic options that may prolong overall survival could also lead to an increase in brain metastases in OC.

REFERENCES

ACKNOWLEDGEMENTS
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Table 1. Demographics and Disease Characteristics of Patients by Presence/Absence of BRCA Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Total (n=40,115)</th>
<th>OC with brain metastases (n=46)</th>
<th>p Value</th>
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<tbody>
<tr>
<td>BRCA wild-type tested (%)</td>
<td>Yes</td>
<td>2223 (4%)</td>
<td>20 (44)</td>
<td>0.05</td>
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<tr>
<td>BRCA wild-type tested (%)</td>
<td>No</td>
<td>18012 (70%)</td>
<td>24 (21)</td>
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<tr>
<td>BRCA-mut tested (%)</td>
<td>Yes</td>
<td>473 (1%)</td>
<td>6 (12)</td>
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<tr>
<td>BRCA-mut tested (%)</td>
<td>No</td>
<td>1563 (4%)</td>
<td>0 (0)</td>
<td></td>
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<tr>
<td>Stage of OC diagnosis, n (%)</td>
<td>I</td>
<td>787 (17%)</td>
<td>2 (4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Stage of OC diagnosis, n (%)</td>
<td>II</td>
<td>1843 (41%)</td>
<td>25 (54)</td>
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<tr>
<td>Stage of OC diagnosis, n (%)</td>
<td>III</td>
<td>876 (19%)</td>
<td>15 (33)</td>
<td></td>
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<tr>
<td>Stage of OC diagnosis, n (%)</td>
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<td>1263 (31%)</td>
<td>8 (14)</td>
<td></td>
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<tr>
<td>Surgery, n (%)</td>
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<td>736 (18%)</td>
<td>4 (56)</td>
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<tr>
<td>Surgery, n (%)</td>
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<td>3287 (78%)</td>
<td>12 (14)</td>
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<td>Patients per institutional</td>
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