Plasma VEGF-A and VEGFR-2 biomarker results from the BEATRICE phase III trial of bevacizumab in triple-negative early breast cancer

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In the comprehensive bevacizumab biomarker program aiming to identify those patients deriving the most substantial benefit from bevacizumab, more than 100 markers have been tested across eight indications in 27 phase III trials. From these exploratory research efforts, a robust dataset has emerged supporting the role for plasma vascular endothelial growth factor (VEGF)-A and plasma VEGF receptor (VEGFR)-2 as potential predictive markers for bevacizumab.

The randomized phase III BEATRICE trial provides the first prospective data on bevacizumab-containing therapy for early breast cancer (BC).

RESULTS

Patient population

Between December 2007 and March 2010, 2051 patients were enrolled. Of these:
- 1272 (62%) consented to the biomarker study.
- 1178 (58%) were included in the biomarker-evaluable population.

Baseline characteristics in the biomarker-evaluable population were balanced between arms (Table 1).

Baseline characteristics

<table>
<thead>
<tr>
<th>Biomarker-evaluable population</th>
<th>Intent-to-treat population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, %</td>
<td>(N=1272)</td>
</tr>
<tr>
<td>White</td>
<td>84</td>
</tr>
<tr>
<td>Black</td>
<td>13</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
</tr>
<tr>
<td>Asian</td>
<td>11</td>
</tr>
<tr>
<td>Black 84 82 75 72</td>
<td>63 65 63 63</td>
</tr>
<tr>
<td>Race</td>
<td>1-3</td>
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<tr>
<td>4</td>
<td>52</td>
</tr>
<tr>
<td>5</td>
<td>52</td>
</tr>
<tr>
<td>Node status</td>
<td>67</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>31</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>66</td>
</tr>
<tr>
<td>Baseline characteristics</td>
<td>41</td>
</tr>
<tr>
<td>Table 1. Baseline characteristics</td>
<td></td>
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</tbody>
</table>

CONCLUSIONS

- Plasma VEGF-A results using the median as the cut-off show neither prognostic nor predictive value.
- However, exploratory analyses using cut-offs more closely representing medium plasma concentrations in metastatic BC suggest a trend toward predictive value.

- A similar pattern was seen for overall survival in the GOG-0218 trial of front-line bevacizumab after surgery in ovarian cancer.3

- Therefore, the possible influence of tumor debulking/resection immediately before treatment and the lower median VEGF-A concentration compared with the metastatic setting (71.8 vs 125.1–129.1 pg/mL) requires further investigation, together with exploration of the impact of differing biology in the adjacent setting.

- As in previous trials across a range of tumor types, baseline plasma VEGFR-2 concentrations were not prognostic.
- However, baseline plasma VEGFR-2 showed potential predictive value for bevacizumab efficacy (Figures 4 and 5):
  - High baseline plasma VEGFR-2 levels were associated with greater IDFS benefit (Table 2 and Figure 3).

- Exploratory analyses using the third quartile as the cut-off (133.6 pg/mL, similar to the median cut-off values in AVADO and AVEREL2,3) showed a trend toward greater IDFS benefit in the subgroup with high baseline plasma VEGF-A levels (Figure 2 and Table 2).

- However, baseline plasma VEGFR-2 showed potential predictive value for bevacizumab efficacy (Figures 4 and 5):
  - High baseline plasma VEGFR-2 levels were associated with greater IDFS benefit.
  - IDFS hazard ratio (HR) = 0.87 (95% confidence interval [CI]: 0.72–1.07; p=0.1810).

- Further exploratory analyses are ongoing to provide better understanding of the BEATRICE dataset and the complex biology of angiogenesis, including additional markers (efficacy and cardiac safety), changes over time, and combination signatures.

Patient population

The median baseline plasma VEGF-A concentration was 77.0 pg/mL.

Baseline plasma VEGF-A

- Baseline plasma VEGF-A showed neither prognostic nor predictive value using the median as the cut-off.
  - High baseline plasma VEGF-A was not associated with greater IDFS benefit than low plasma VEGF-A concentrations (Figure 2).

- Exploratory analyses using the third quartile as the cut-off (133.6 pg/mL, similar to the median cut-off values in AVADO and AVEREL2,3) showed a trend toward greater IDFS benefit in the subgroup with high baseline plasma VEGF-A levels (Figure 2 and Table 2).

- However, baseline plasma VEGFR-2 showed potential predictive value for bevacizumab efficacy (Figures 4 and 5):
  - High baseline plasma VEGFR-2 levels were associated with greater IDFS benefit.
  - IDFS hazard ratio (HR) = 0.87 (95% confidence interval [CI]: 0.72–1.07; p=0.1810).

REFERENCES


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