Retrospective Pooled Analysis to Assess Correlation Between Time to Progression and Overall Survival in Patients With Breast Cancer

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BACKGROUND
- Increased overall survival (OS) is the gold standard for clinical benefit in breast cancer patients, but survival data from randomized clinical trials (RCTs) are often insensitive due to subsequent treatment.
- Surrogate measures showing lengthened time to tumor progression (TTP) and/or progression-free survival (PFS) in advanced disease, and disease-free survival (DFS) in the adjuvant setting are clinically valid endpoints and may be acceptable for drug approval.

METHODS
- A structured literature search was conducted based on prespecified inclusion/exclusion criteria.
- An electronic literature search was conducted using PubMed (July 20, 2004).
- Individual citations were downloaded into a Reference Manager database.
- Abstracts and full-text articles were retrieved and examined for relevance.
- Inclusion criteria:
  - RCTs,
  - Confirmed metastatic or advanced breast cancer and/or recurrence,
  - English language,
  - Full-text articles available.
- Outcomes measured must include survival AND tumor progression.
  - Number of deaths, median (mean) patient survival.
- English language,
- Abstracts and full-text articles were retrieved and examined for relevance.
- Individual citations were downloaded into a Reference Manager database.
- Others provided a definition associated with the term PFS.
- Findings suggest that the relationship between disease progression and survival varies by factors such as tumor subtype.

RESULTS

CONCLUSIONS
- In various cancers, researchers have demonstrated the relationship between disease progression and OS by pooling data across studies:
  - Metastatic colorectal cancer1
  - Colon cancer in the adjuvant setting2
  - Non-small cell lung cancer3
- We explored the association between disease progression endpoints and survival in metastatic breast cancer using published data.
- These preliminary results are consistent with findings in other settings are clinically valid endpoints and may be acceptable for benefit in cancer patients, but survival data from randomized clinical trials (RCTs) are often insensitive due to subsequent treatment.
- The simple analysis presented here has limitations. It ignores the original randomization for each study and model that data from different treatment arms in the same study are not related. Its apparent simplicity, both for explaining the approach and for the reader, may over-simplify matters, but the present analysis underscores the magnitude of relationship between endpoints.

REFERENCES

CONTACT INFORMATION
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Figure 1. Residual Regressions for Retrospective Studies

Figure 2. Regression of OS on TTP/PFS

Figure 3. Regression of OS on TTP/PFS

Table 1. Summary of Studies Included

<table>
<thead>
<tr>
<th>Study ID Number</th>
<th>Number of Patients</th>
<th>Number of Studies</th>
<th>Type of TTP/PFS</th>
<th>Type of OS</th>
<th>Correlation</th>
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<td>50</td>
<td>1</td>
<td>TTP only</td>
<td>OS</td>
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<tr>
<td>2</td>
<td>100</td>
<td>1</td>
<td>PFS only</td>
<td>OS</td>
<td>0.25</td>
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Table 2. Included Studies

<table>
<thead>
<tr>
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Figure 3. Regression of OS on TTP/PFS

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A scatter plot of OS vs TTP/PFS is shown with a regression line. The correlation coefficient is 0.31.*