Cost Drivers of a Hospital Acquired and Ventilator Acquired Bacterial Pneumonia (HABP/VABP) Phase Three Clinical Trials

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Introduction

Hospital Acquired Bacterial Pneumonia (HABP) and Ventilator Acquired Bacterial Pneumonia (VABP) combined—Nosocomial pneumonia, NP or healthcare associated pneumonia (HCAP) are acute infections that occur in hospitalized patients. A hospital stay of 48 hours or more will expose patients to potential infections with a variety of gram-positive and gram-negative bacteria, many of which have become antibiotic resistant.[1]

Studies indicate that the prevalence of NP has been rising.[2] Many of these cases are caused by antibiotic resistant bacteria, increasing the demand for new antibiotics.[3] However, NP clinical trials are very costly to conduct given protocol complexities, multiple pathogens, and difficulty recruiting and retaining patients. NP drug candidates under development are therefore more likely to be discontinued.[4,5]

A new study conducted by the Tufts Center for the Study of Drug Development (Tufts CSDD) and the Clinical Trials Innovation Initiative at Duke University (CTTI) evaluates the drivers of HABP/VABP direct and indirect clinical trial costs and identifies opportunities to lower these costs. It is hoped that the results of this study increase biopharmaceutical company incentives to continue to develop HABP/VABP drugs.

Methodology

Tufts CSDD, in collaboration with CTTI developed a comprehensive, detailed map of direct and indirect cost elements. Primary cost elements include per-patient direct procedure costs, per-trial and per-site costs:

- Personal Direct Costs
  - Site and Clinical Supply Costs
  - Clinical Supplies Costs
  - IT Charges for EDC
  - Data Entry
  - Translation
- Trial Indirect Costs
  - Informed Consent
  - Clinical Trial Insurance
  - Screen Fails

INDIRECT COST ELEMENTS

- Upper Management
  - Vice President
  - Executive (Medical) Director
  - Associate Director
- Biostatistics Manager
- Data Costs

Upper Management

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METHODS

TUFTS CSDD determined the fully depreciated cost of a HABP/VABP phase II clinical trial with 1,000 patients and 200 global sites to be, on average, $58,400 per patient.

Phase III HABP/VABP clinical trials are $9,000 per-patient more expensive than phase II oncology clinical trials, and $34,000 per-patient more expensive than endocarditis studies.

Key variables affecting the cost of a typical phase three HABP/VABP trial can be stratified as the number of patients, the number of sites, procedure costs, screen failure rates, the cost of screen fails, and the cost of patient recruitment.

RESULTS

AVERAGE COST PER PATIENT FOR ENDOCRINE, ONCOLOGY, AND HABP/VABP PHASE III CLINICAL TRIALS

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Per-Patient Direct Cost ($1000)</th>
<th>Per-Trial Direct Cost ($1000)</th>
<th>Indirect Cost ($1000)</th>
<th>Total Cost Per Patient ($1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine</td>
<td>$9.5</td>
<td>$42.3</td>
<td>$5.8</td>
<td>$57.5</td>
</tr>
<tr>
<td>Oncology</td>
<td>$18.2</td>
<td>$61.8</td>
<td>$7.5</td>
<td>$87.4</td>
</tr>
<tr>
<td>HABP/VABP</td>
<td>$86.1</td>
<td>$20.1</td>
<td>$3.3</td>
<td>$89.6</td>
</tr>
</tbody>
</table>

IMPRINT OF CHANGING KEY COST DRIVER AT A TIME FOR HABP/VABP CLINICAL TRIALS

<table>
<thead>
<tr>
<th>Variable</th>
<th>HABP/VABP</th>
<th>Oncology</th>
<th>Endocrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Patients (+/- 100 patients)</td>
<td>$78</td>
<td>$86</td>
<td>$94</td>
</tr>
<tr>
<td>Number Patients (+/- 100 patients)</td>
<td>$80</td>
<td>$88</td>
<td>$96</td>
</tr>
<tr>
<td>Number Patients (+/- 100 patients)</td>
<td>$82</td>
<td>$90</td>
<td>$100</td>
</tr>
<tr>
<td>Number Patients (+/- 100 patients)</td>
<td>$84</td>
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<td>$102</td>
</tr>
<tr>
<td>Number Patients (+/- 100 patients)</td>
<td>$86</td>
<td>$94</td>
<td>$104</td>
</tr>
<tr>
<td>Number Patients (+/- 100 patients)</td>
<td>$88</td>
<td>$96</td>
<td>$106</td>
</tr>
</tbody>
</table>

LIMITATIONS

- Assumptions of cost variables for sensitivity analysis is limited (e.g. procedure costs)
- Some cost elements are average costs across all therapeutic areas
- Assuming that proportion of sites by country is the same as proportion of patients by country

CONCLUSIONS

- Opportunities to lower the high costs of HABP/VABP clinical trials exist.
- The cost of screen fails, as well as screen failure rates are the main drivers of cost for a phase III HABP/VABP trial.
- Future studies are looking to assess best practices for protocol design in order to decrease costs while maintaining scientific rigor.

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