Poster T 08

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

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CLINICAL TRIALS TRANSFORMATION INITIATIVE

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 Transformation 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 mapping of direct and indirect cost elements. Primary cost elements include per-patient direct procedure costs, per-trial and per-site costs:

Per-Patient Direct Costs
- Patient Costs

Per-Trial Direct Costs
- Personnel Costs (Pharmaceutical Company and Investigative Site)
- Site and Clinical Supply Costs; Trial Insurance
- Printing / Paper / Data Costs

Per-Trial Indirect Costs
- Upper Management Time
- Overhead Costs
- Misc. Costs

Figure 1. The Primary Cost Elements

Tufts CSDD gathered benchmark data to create a model calculating a fully-loaded (direct and indirect) cost profile of a typical phase three HABP/VABP clinical trial. Costs for phase III oncology trials and endocrine trials were also calculated for comparison. Data were gathered from the following:

- Internal databases provided site and subject (patient) data
- Medidata Solutions provided protocol and site cost data
- Oracle Clinical provided benchmarking costs for HABP/VABP
- IMS Health provided country-site distribution data
- PMG, and CenterWatch provided site cost estimates (e.g. IRB fees, case report form fees; etc.)
- FDA, Centerphase Solutions and Mckane et al [3] provided patient screen-failure rates and randomization rates.
- Data involving printing costs, translation costs, and server costs for electronic data capture (EDC), and clinical trial insurance costs were gathered from companies providing these services and solutions.

Assumptions provided on study duration were derived from industry experts. This study was conducted from November, 2014 to May, 2015.

Methodology

PER-PATIENT DIRECT COST ELEMENTS

- Patient Recruitment
- Patient Retention (i.e. compensation)
- Informed Consent
- Clinical Trial Insurance
- Screen Fails
- Procedures
- Lab Tests
- Query Resolution
- Data Entry

PER-TRIAL DIRECT COST ELEMENTS

Personnel Costs
- Sponsor Personnel
  - Clinical Pharmacology
  - CRO/Site Contract Management
  - Document Manager
  - Clinical Research Associate
  - Physician
  - Statistical Programmer
  - Study Manager
  - Pharmaceutical Technician
  - Product Development
- Site Personnel
  - Principal Investigator
  - Co-Investigator
  - Research Nurse / Study Coordinator
  - Technician
  - Other Administration
  - Recruitment Specialist
  - Microbiologist
  - Regulatory Affairs
  - Pharmacist / Pharmacy tech

Site and Clinical Supply Costs
- IRB Fees (Local)
- Amendment Fees
- Record Keeping and Storage
- Site Recruitment Costs (marketing)
- PI Training / Travel Costs
- Meeting costs for clinical travel team (venue, food, travel)
- Clinical Supply Costs (for this model is fixed)
  - Manufacturing
  - Comparator
- Trial Insurance Costs

Printing / Paper / Data Costs
- Investigator Brochure
  - Printing
  - Translation
- Study Protocol
  - Printing
  - Translation
- Informed Consent
  - Printing
  - Translation
- Case Report Form
  - Printing
  - Translation
- Data Costs
  - Server charges for EDC
  - IT Charges for EDC
  - Storage Costs
  - Data Entry Costs

Figure 2. List of Per-Trial and Per Site Cost Elements.

INDIRECT COST ELEMENTS

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

Overhead Costs
- Travel and Meetings
- Depreciation (equipment)
- Depreciation (buildings)
- Other infrastructure costs
- Material and office supplies
- IT costs

Other Costs
- Administration Costs
- Training and Professional Development
- Employee Benefits

Figure 3. List of Indirect Cost Elements

STUDY ASSUMPTIONS

Variable	HABP/VABP	Oncology	Endocrine
Total Sites (all locations)	200 sites	279 sites	123 sites
Total Subjects (all locations)	1,000 subjects	448 subjects	582 subjects
Total Number of Countries	52 countries	74 countries	47 countries
Randomization Rate	1 patients randomized per 100 screened	25 patients randomized per 100 screened	45 patients randomized per 100 screened

Figure 4. Study Assumptions.
Site and patient (subject) assumptions based on internal Tufts CSDD databases.

Results

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

Therapeutic Area	Per-Patient Direct Cost ($000)	Per-Trial Direct Cost ($000)	Indirect Cost ($000)	Total Cost Per Patient ($000)
Endocrine	$9.5	$42.3	$5.8	**$57.5**
Oncology	$18.2	$61.8	$7.5	**$87.4**
HABP/VABP*	$66.1	$20.1	$3.3	**$89.6**

Figure 5. Average cost-per-patient for a Phase III Endocrine, HABP/VABP, and Oncology trial.
*HABP/VABP trials may run to a maximum of $165,000 per patient under the same assumptions (1,000 patients; 200 sites; 32 countries). Maximum provided by Oracle Clinical. Per-patient direct costs are high for HABP/VABP due to high screen failure rate.

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

Figure 6. Cost Drivers: Changing One Driver
Using current assumptions: cost is $89,600 per patient. Assuming geographic distribution of patients is equal to the geographic distribution of sites (10% of patients in the US). Increasing the number of patients decreases costs as the number of patients outside of the US (in less expensive regions) increases.

IMPACT OF CHANGING MULTIPLE COST DRIVERS AT A TIME FOR HABP/VABP CLINICAL TRIALS

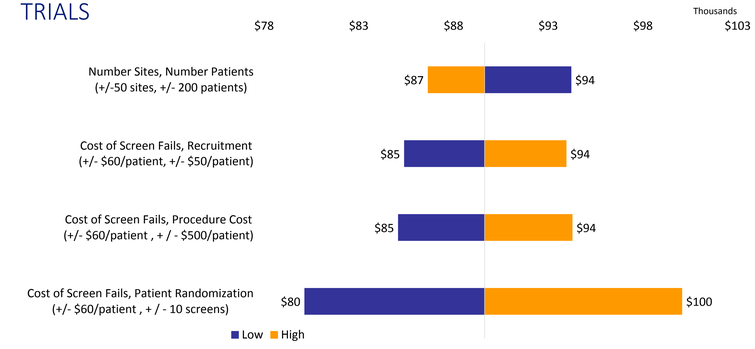

Figure 7. Cost Drivers: Changing Multiple Drivers
Using current assumptions: cost is $89,600 per patient. Assuming geographic distribution of patients is equal to the geographic distribution of sites (10% of patients in the US).

Summary

- Tufts CSDD determined the fully-loaded cost of a HABP/VABP phase III clinical trial with 1,000 patients and 200 global sites to be, on average, $89,600 per patient.
- Phase III HABP/VABP clinical trials are $9,000 per-patient more expensive than phase III oncology clinical trials, and $34,000 per-patient more expensive than endocrine studies.
- Key variables affecting the cost of a typical phase three HABP/VABP trial can be stratified are the number of patients, the number of sites, procedure costs, screen failure rates, the cost of screen fails, and the cost of patient recruitment.

Limitations

- Assessment of certain variables for sensitivity assessment 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
- Assuming that site-patient percentage is the same for HABP/VABP, oncology and endocrine trials
- Assuming internal work effort is the same for HABP/VABP, oncology and endocrine trials

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 asses best practices for protocol design in order to decrease costs while maintaining scientific rigor.

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