Introduction

• Observations at the authors' institutions and by Dilts, et al (ASCO 2008, abstr 6534) indicate a high percentage of industry and cooperative group sponsored therapeutic clinical trials with minimal enrollment.

• We observed most of the enrollment from a small proportion of these trials.

• Start-up and regulatory maintenance is significant and unrelated to enrollment.

• We examined 7-years of center data and determined significant restructuring was necessary in the criteria by which trials were selected for activation.

Methods

• Accrual data to industry- and cooperative group-sponsored therapeutic clinical trials


• Pre-specified criteria: trials open once; categorized by center, enrollment levels, phase I vs. phase II-III and “rare” diseases.

• Pediatric trials excluded.

• Data aggregated by PercipEnz Technologies, Inc.

Results: Protocol Performance

- 3378 Protocols
- 8977 Patients

<table>
<thead>
<tr>
<th># Protocols per Enrollment Level</th>
<th>Coop</th>
<th>Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Accrual</td>
<td>887</td>
<td>915</td>
</tr>
<tr>
<td>1 Patient</td>
<td>196</td>
<td>172</td>
</tr>
<tr>
<td>2 Patients</td>
<td>132</td>
<td>150</td>
</tr>
<tr>
<td>&gt; 2 Patients</td>
<td>386</td>
<td>550</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Enrollment per Enrollment Level</th>
<th>Coop</th>
<th>Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>No accrual</td>
<td>4.6%</td>
<td>3.5%</td>
</tr>
<tr>
<td>1 Patient</td>
<td>6.6%</td>
<td>6.0%</td>
</tr>
<tr>
<td>2 Patients</td>
<td>88.8%</td>
<td>90.5%</td>
</tr>
</tbody>
</table>

Conclusions

• 28% of industry and cooperative group sponsored therapeutic clinical trials, in adults, account for 90% of enrollment to these trials.

• Over 50% of these trials did not enroll any patients.

• Significant resources are used on trials that do not contribute to overall enrollment.

• Effective rules governing selection of adult industry and cooperative group trials are needed.

• Protocol selection rules implemented at two cancer centers have virtually eliminated the number of trials with no enrollment thus re-directing valuable resources to useful activities without a significant adverse effect on overall enrollment.

Protocol Selection Criteria

Industry-sponsored trials and cooperative group trials for adults must accrue at least 3 patients over the time-period that the trial will be open to enrollment.

Principal investigators must demonstrate either:
- adequate accrual history to similar trial(s) or
- proof that they will see at least 12 potentially eligible patients over the time that the trial will be open to enrollment.

Methods

• Accrual data to industry- and cooperative group-sponsored therapeutic clinical trials


• Pre-specified criteria: trials open once; categorized by center, enrollment levels, phase I vs. phase II-III and “rare” diseases.

• Pediatric trials excluded.

• Data aggregated by PercipEnz Technologies, Inc.
Clinical Trial Metrics: Protocol Performance and Resource Utilization from 14 Cancer Centers

– Henry J. Durivage, Pharm.D., The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey (UMDNJ), New Brunswick, NJ
– Kerry D. Bridges, RN, MBA, Indiana University Simon Cancer Center, Indianapolis, IN
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• We observed most of the enrollment from a small proportion of these trials.
• Start-up and regulatory maintenance is significant and unrelated to enrollment.
• We examined 7-years of center data and determined significant restructuring was necessary in the criteria by which trials were selected for activation.
Methods

• Accrual data to industry- and cooperative group-sponsored therapeutic clinical trials was initially obtained from 14 U.S. cancer centers and recently expanded to 16 cancer centers

• Data for the 3-year period from 2005 through 2007 was analyzed initially. The dataset was expanded to include 2008. Trials closed in each calendar year comprised the dataset.

• The majority of the studies were phase II or phase III.

• Pediatric clinical trials were excluded from the dataset.
Results

- 3378 therapeutic clinical trials (1591 cooperative group and 1787 industry)
- 8977 patients enrolled (4012 cooperative group and 4965 to industry)
- 1802 (53.3%) did not enroll any patients
  - 887 (55.7%) cooperative group
  - 915 (51.2%) industry
- 640 (18.9%) trials enrolled 1 or 2 patients
- Only 936 (27.7%) trials enrolled > 2 patients and these trials accounted for 89.7% of the total enrollment.
- Excluding therapeutic clinical trials of hematologic malignancies did not significantly alter the results.
### Protocol Performance
(Industry & Cooperative Group protocols, 2005-2008, n=3378)

<table>
<thead>
<tr>
<th>Protocol Enrollment Levels (e.g., 1 patient/protocol, etc.)</th>
<th>Coop Group</th>
<th>Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Accrual</td>
<td>887 (56%)</td>
<td>915 (51%)</td>
</tr>
<tr>
<td>1 Patient</td>
<td>186 (12%)</td>
<td>172 (10%)</td>
</tr>
<tr>
<td>2 Patients</td>
<td>132 (8%)</td>
<td>150 (8%)</td>
</tr>
<tr>
<td>&gt;2 Patients</td>
<td>386 (24%)</td>
<td>550 (31%)</td>
</tr>
</tbody>
</table>

1802 of 3378 cooperative group and industry protocols did not enroll any patients.
Protocol Performance
(Industry and Cooperative Group protocols, 2005-2008, n=3378)

72.2% of cooperative group and industry protocols enroll less than 3 patients.

<table>
<thead>
<tr>
<th>Protocol Enrollment Levels (e.g., 1 patient/protocol, etc.)</th>
<th>Coop</th>
<th>Industry</th>
<th>Coop + Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Accrual</td>
<td>55.7%</td>
<td>51.2%</td>
<td>53.3%</td>
</tr>
<tr>
<td>1-2 pts/trial</td>
<td>20.0%</td>
<td>18.0%</td>
<td>18.9%</td>
</tr>
</tbody>
</table>
Protocol Enrollment Levels
Effect on Overall Enrollment (8977 patients, 3378 protocols)

<table>
<thead>
<tr>
<th>Protocol Enrollment Levels</th>
<th>Coop</th>
<th>Industry</th>
<th>Coop. + Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 pt/trial</td>
<td>186</td>
<td>172</td>
<td>358</td>
</tr>
<tr>
<td>2 pts/trial</td>
<td>264</td>
<td>300</td>
<td>564</td>
</tr>
<tr>
<td>&gt; 2 pts/trial</td>
<td>3562</td>
<td>4493</td>
<td>8055</td>
</tr>
</tbody>
</table>

8055 of 8977 patients (89.7%) are enrolled to the protocols with >2 patients.
Cancer Center # 9
(Industry & Cooperative Group trials, 2005-2008, n=277)

100 (36.1%) of 277 trials did not enroll any patients.

<table>
<thead>
<tr>
<th>Protocol Enrollment Levels</th>
<th>Coop</th>
<th>Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Accrual</td>
<td>53 (50.5%)</td>
<td>47 (27.3%)</td>
</tr>
<tr>
<td>1 pt/trial</td>
<td>14</td>
<td>19</td>
</tr>
<tr>
<td>2 pts/trial</td>
<td>6 (30.5%)</td>
<td>22 (40.8%)</td>
</tr>
<tr>
<td>&gt; 2 pts/trial</td>
<td>32</td>
<td>84</td>
</tr>
</tbody>
</table>
Cancer Center #9
Effect on Overall Enrollment (1040 patients, 277 protocols)

Protocol Enrollment Levels

<table>
<thead>
<tr>
<th></th>
<th>Coop</th>
<th>Industry</th>
<th>Coop. + Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 pt/trial</td>
<td>14</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>2 pts/trial</td>
<td>12</td>
<td>44</td>
<td>56</td>
</tr>
<tr>
<td>&gt; 2 pts/trial</td>
<td>259</td>
<td>692</td>
<td>951</td>
</tr>
</tbody>
</table>

951 of 1040 (91%) patients enrolled are to the protocols with >2 patients.
Resource Impact*
Industry & Cooperative Group Trials with No Enrollment

• Assumptions, per trial:
  – Start-up: study tools, pre-initiation and initiation meetings, etc. 60 hours (cooperative group), 100 hours (industry)
  – Regulatory: amendments (3), continuing reviews (2), OSRs (100 industry, 5 cooperative group)
  – Off-site investigator-meetings: 5% of the industry trials
  – Patients screened: 5 per trial, 2 hours each

Resource Impact
Industry & Cooperative Group Trials with No Enrollment

• 915 industry trials and 887 cooperative group trials

• Clinical Trials Office (CTO) staff effort:
  – 287,930 hrs, 16 centers, 4 years
  – 4,500 hrs (2.9 FTE) per center per year
  – 46 people per year across 16 centers

• Net Loss: $81,000 per center per year
  (assumes $6,000 start-up income to CTO for 915 industry trials)
Resource Impact: Cancer Center #9
Industry & Cooperative Group Trials with < 2 Patients Enrolled

• Cooperative group trials:
  – 53 trials with no enrollment
  – 14 trials with 1 patient, 6 trials with 2 patients

• Industry trials:
  – 47 trials with no enrollment
  – 19 trials with 1 patient, 22 trials with 2 patients

• Enrollment to trials with ≤ 2 patients:
  – 8.6% of total enrollment

• Research office staff effort:
  – Approximately 7.5 FTE per year

• Net Loss: $245,000 per year
Cost of Clinical Trials
Under-performing Trials, 2005-2008

Annual lost income associated with industry and cooperative group clinical trials enrolling < 2 patients per trial.
Note: these trials account for approximately 10% of total accrual.

<table>
<thead>
<tr>
<th></th>
<th>All Centers</th>
<th>Center # 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>No accrual</td>
<td>$81,000</td>
<td>$113,000</td>
</tr>
<tr>
<td>1 pt/trial</td>
<td>$70,000</td>
<td>$67,000</td>
</tr>
<tr>
<td>2 pts/trial</td>
<td>$60,300</td>
<td>$65,000</td>
</tr>
</tbody>
</table>
Follow-Up

- Rules governing selection of industry- and cooperative group-sponsored therapeutic clinical trials for activation were implemented at the Cancer Institute of New Jersey in January 2008 and at the Indiana University Simon Cancer Center in October 2008.

- Protocol selection rules are enforced by each center’s Protocol Review and Monitoring System.
Protocol Submission Policy
Implemented by CINJ and IU

• Industry-sponsored trials and cooperative group trials for adults must accrue at least 3 patients over the time-period that the trial will be open to enrollment.

• Principal investigators must demonstrate either:
  – adequate accrual history to similar trial(s) or
  – proof that they will see at least 12 potentially eligible patients over the time that the trial will be open to enrollment.
CINJ Protocol Selection Rules
Early Effect in Phase II-III Trials

Industry and adult cooperative group phase II-III trials. Trials approved in 2008-2009 and open to enrollment for > 3 months.
IU Protocol Selection Rules
Early Effect in Phase II-III Trials

Conclusions

• Approximately 90% of the accrual to industry- and cooperative group-sponsored therapeutic clinical trials is from the 26% of the trials enrolling > 2 patients/trial.

• Significant resources are used on therapeutic clinical trials that do not contribute significantly to overall accrual.

• Effective rules governing selection of industry- and cooperative group-sponsored therapeutic clinical trials for activation are needed.

• Effective rules will enable centers to re-direct valuable resources to useful activities without adverse effect on overall enrollment.