Empowering Study Teams to Improve Clinical Trial Activation Timelines

Erica J. Rocco, BS, CCRP; Nicholas A. Licht, MBA; Nicole L. O’Dell, MLS, PhD; Tesheia Johnson, MBA, MHS; Rhoda Arzoomanian, MSM, BSN, RN

Yale School of Medicine - Yale Center for Clinical Investigation (YCCI)

Background
In 2016, the Yale School of Medicine and Yale Cancer Center (YCC) identified clinical trial activation timelines as a strategic improvement opportunity to:
• advance medical care and research,
• enhance Yale’s position as a competitive Medical School and Comprehensive Cancer Center, and
• expand patient access to clinical trials within the Yale Medicine network.

An initial activation analysis included input from more than 100 stakeholders, which resulted in the identification of 43 areas for improvement and the creation of an internal Protocol Activation (PAct) Team. A pilot of all YCC trials opened since December 2017 has utilized newly established processes and metric tracking (over 130 protocols to-date).

Goals
• Empower research teams to improve start-up timelines in order to consistently achieve clinical trial activation within 90 calendar days from Protocol Review Committee (PRC) submission.
• Optimize 13 individual activation sub-processes
  • Establish tasks that start and end each sub-process
  • Identify co-dependencies with other sub-processes
  • Review actual and target durations for each sub-process
• Decrease overall time to activation (TTA), to achieve current target timelines (Table 1)

Table 1: Target calendar days from PRC submission to open to accrual

<table>
<thead>
<tr>
<th>Agreement Type</th>
<th>IRB</th>
<th>Business Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Existing Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>New Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Cooperative Group/NCI CIRB</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agreement Type</th>
<th>IRB</th>
<th>Business Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Existing Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>New Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Cooperative Group/NCI CIRB</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
</tbody>
</table>

Methods
Sub-process workflows translated into OnCore Activation Task Lists (Table 2)

Table 2: OnCore Activation Task Lists [Number of Tasks]

<table>
<thead>
<tr>
<th>Task List</th>
<th>Number of Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Decision</td>
<td>5</td>
</tr>
<tr>
<td>Feasibility</td>
<td>10</td>
</tr>
<tr>
<td>Consent Form</td>
<td>4</td>
</tr>
<tr>
<td>OnCore Build</td>
<td>36</td>
</tr>
<tr>
<td>Beacon Build</td>
<td>9</td>
</tr>
<tr>
<td>Protocol Review Committee (PRC)</td>
<td>6</td>
</tr>
<tr>
<td>Radiation Safety Committee</td>
<td>6</td>
</tr>
<tr>
<td>Institutional Biosafety Committee</td>
<td>4</td>
</tr>
<tr>
<td>Human Research Protection Program</td>
<td>3</td>
</tr>
<tr>
<td>Activation</td>
<td>20</td>
</tr>
</tbody>
</table>

Goals
• Empower research teams to improve start-up timelines in order to consistently achieve clinical trial activation within 90 calendar days from Protocol Review Committee (PRC) submission.
• Optimize 13 individual activation sub-processes
  • Establish tasks that start and end each sub-process
  • Identify co-dependencies with other sub-processes
  • Review actual and target durations for each sub-process
• Decrease overall time to activation (TTA), to achieve current target timelines (Table 1)

Table 1: Target calendar days from PRC submission to open to accrual

<table>
<thead>
<tr>
<th>Agreement Type</th>
<th>IRB</th>
<th>Business Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Existing Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>New Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Cooperative Group/NCI CIRB</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agreement Type</th>
<th>IRB</th>
<th>Business Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Master Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Existing Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>New Contract Agreement</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
<tr>
<td>Cooperative Group/NCI CIRB</td>
<td>Internal IRB</td>
<td>Master/Existing/New [3]</td>
</tr>
</tbody>
</table>

Outcomes
• Creation of an internal Protocol Activation (PAct) Team
• Implementation of 19+ new activation task lists in OnCore
• Development of data field definitions for over 100 task fields
• Concurrent PRC and HRPP submissions for industry sponsored and authored protocols
• Regular meetings with sub-process owners, regulatory managers, and disease-aligned study teams to ensure a bidirectional flow of information

There has been a notable decrease in activation timelines since the initiation of the YCC Pilot with the PAct Team. Metrics show that between 2017 and 2018, the overall clinical trial activation timelines decreased by 19 calendar days. As of June 2019, the TTA median for protocols submitted to PRC in 2019 is 96 calendar days.

Future Direction
• Continue working with sub-process owners and disease teams to identify and address additional areas for improvement
• Continue attending oncology research team meetings to present metrics and identify bottlenecks for pending trials in real time
• Currently finalizing a number of additional process improvements, based on stakeholder feedback:
  • Implementing Centralized Medicare Coverage Analysis
  • Streamlining submission processes to ancillary committees
  • Optimizing treatment plans in Epic Beacon
  • Tracking of IND submissions associated with investigator-initiated trials
  • Expanding access to dashboards and enhance metric reporting

The Protocol Activation (PAct) project is an ongoing endeavor which continues to evolve based on the data trends. As the project matures, the data will more fully demonstrate the impacts on study activation timelines.