Assessment of clinical trials in oncology: An evaluation of 40,969 interventional trials on clinicaltrials.gov

BACKGROUND
ClinicalTrials.gov is one of the largest databases of clinical research, comprising over 150,000 trials in 170 countries. With over 50 million page views a month, it is the most utilized source for clinical trial information worldwide. While the database was initially created as a result of the US Food and Drug Administration (FDA) Modernization Act of 1997, the FDA made registration a requirement as of 2007 for all new clinical trials expected to contribute to an FDA submission. In addition, the International Committee of Medical Journal Editors mandates that all trials be included in a public registry as a requirement for publication of results in peer-reviewed medical journals.

Throughout a collaboration between the FDA and Duke University, as part of the Clinical Trials Transformation Initiative (CTTI), the goal of this project is to systematically summarize the relevant information in the ClinicalTrials.gov database to understand the full portfolio of clinical trials and the potential gaps therein. In this project we describe the portfolio of studies enrolling patients with cancer in ClinicalTrials.gov.

METHODS
- A dataset comprising 46,946 clinical trials was downloaded from ClinicalTrials.gov on September 27, 2013, in XML format and transformed to a relational database for analysis.
- To regroup studies into clinical specialties, the team developed a methodology using the National Library of Medicine’s (NLM) MeSH thesaurus (2010 version) combined with information from other fields of the database.
- A process was developed for annotating, validating, and implementing disease conditions (MeSH and non-MeSH terms) to create specialty databases.
- Non-MeSH condition terms were selected from interventional studies registered after September 2007 that appeared in five or more studies.
- Selected disease condition terms (MeSH and non-MeSH) were reviewed and annotated by faculty and clinicians within each clinical discipline at Duke University Medical Center.
- Ultimately, disease conditions provided by submitters to the ClinicalTrials.gov database (CONDITIONS) were combined with MeSH condition terms (CONDITION, BROWSE) generated by the NLM algorithm to generate a summary algorithm that categorized trials in ClinicalTrials.gov by disease specialty, as outlined in Figure 1.

RESULTS
- Of 46,946 interventional studies registered between September 2007 and September 2010, 6,241 (13%) focused on oncology, one of the highest percentages among all specialties.
- Compared with other specialties, oncology trials were more likely to be early phase, as shown in Figure 2 (84% phase 1 or 2 (vs. 56% in non-oncology).
- The majority of oncology trials were also single-arm (86% vs. 25%) and unblinded (88% vs. 47%), while the types of interventional and regional distribution of trials were similar between oncology and non-oncology trials (Table 1).
- In the subset of trials reporting actual accrual, oncology studies averaged 43 patients and non-oncology 60 patients.
- In terms of eligibility criteria, maximum age cut-offs were less frequently reported in oncology (35% vs. 65%), with the most common exclusion being age > 70 years.
- Oncology trials were more likely to have a data monitoring committee (30% vs. 2%), although this data point is more likely to be missing in oncology than non-oncology (34% vs. 12%), possibly affecting these results.

LIMITATIONS
- This full mapping algorithm is intentionally broad and inclusive; therefore, some oncology-related studies may be included.
- There is also heterogeneity in interpretation of the data fields by those entering responses into ClinicalTrials.gov, and the data were not independently verified in this analysis.

CONCLUSIONS
- The ClinicalTrials.gov database provides a unique opportunity to understand the breadth of interventional trials in oncology.
- Oncology trials are more frequently smaller, early-phase, single-arm, and unblinded.
- These data identify strengths and weaknesses in trial design, patient populations, and evidence development in oncology that need to be carefully considered as we enhance focusing research on oncology and comparative effectiveness research.
- Subsequent analyses will focus on sub-regions: these results by cancer type and impact of trial sponsor on the portfolio, to identify opportunities for improving the evidence development process in cancer.

Figure 1 – Analysis methodology (provided by A. Tasneem)

Table 1 – Comparison of oncology and non-oncology trial characteristics

<table>
<thead>
<tr>
<th>Categories</th>
<th>Oncology (n = 9,040)</th>
<th>Other medicine specialties (n = 29,879)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention model</td>
<td>Single arm</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>Parallel</td>
<td>33%</td>
</tr>
<tr>
<td>Masking</td>
<td>Double blind</td>
<td>8%</td>
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<tr>
<td>Purpose of intervention</td>
<td>Supportive care</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Basic science</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>Health services</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>Cancer screening</td>
<td>1%</td>
</tr>
<tr>
<td>Regional distribution*</td>
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<td>65%</td>
</tr>
<tr>
<td></td>
<td>South America</td>
<td>3%</td>
</tr>
<tr>
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<td>Asia</td>
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<tr>
<td></td>
<td>Middle East</td>
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</tr>
<tr>
<td></td>
<td>Africa</td>
<td>1%</td>
</tr>
</tbody>
</table>

* Studies may enroll subjects in more than one region

Figure 2 – Cumulative percent of trials in oncology vs. non-oncology by phase

CONTACT INFORMATION
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