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

BR Hirsch, MD[1,3], RM Califf, MD[2], A Tasneem, PhD[3], K Chiswell, PhD[3], JR Horton, MS[3], J Bolte[2], KA Schulman, MD[3], AP Abernethy, MD[1]

[1]Duke Cancer Institute, [2]Duke Translational Medicine Institute, [3]Duke Clinical Research Institute, Durham, NC

BACKGROUND

ClinicalTrials.gov is one of the largest databases of clinical research, comprising over 100,000 trials in 170 countries. With over 50 million page views a month, it is also 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.

Through 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.

ACKNOWLEDGMENTS

Deborah Zarin, MD
Director, ClinicalTrials.gov
National Library of Medicine, National Institutes of Health

Nick Ide, MS
National Library of Medicine, National Institutes of Health

Principal Investigator:
Robert M. Califf, MD
Director, Duke Translational Medicine Institute

Financial support provided by grant U19 FD003800 from the U.S. Food and Drug Administration awarded to Duke University for the Clinical Trials Transformation Initiative (https://www.trialstransformation.org/).

CONTACT INFORMATION

Bradford Hirsch, MD
Bradford.hirsch@duke.edu
919-627-1003

DCRI COMMUNICATIONS • MAY 2011

METHODS

- A dataset comprising 96,346 clinical trials was downloaded from ClinicalTrials.gov on September 27, 2010, in XML format and transitioned to a relational database to facilitate 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 datasets.
  - 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 dataset (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.
- This algorithm will be made publically available as a part of the CTTI project once complete and verified. For this analysis, a comparison was made between studies categorized as oncology and non-oncology in the database.

RESULTS

- Of 40,969 interventional studies registered between September 2007 and September 2010, 9,040 (22%) 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 I or II in oncology vs. 52% in non-oncology).
- The majority of oncology trials were also single-arm (65% vs. 23%) and unblinded (88% vs. 47%), while the types of intervention 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 42 patients and non-oncology 60 patients.
- In terms of eligibility criteria, maximum age cut-offs were less frequently reported in oncology (25% vs. 60%), with the most common exclusion being age > 70 years.
- Oncology trials were more likely to have a data monitoring committee (DMC) (53% vs. 38%), although this data point is more likely to be missing in oncology trials than non-oncology (30% vs. 15%), possibly affecting these results.

LIMITATIONS

- The NLM tagging algorithm is intentionally broad and inclusive; therefore, some non–oncology-related studies may be included.
- There is wide 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 unmasked.
- These data identify strengths and weaknesses in trial design, patient populations, and evidence development in oncology that need to be carefully considered in an era of increasing focus on research design and comparative effectiveness research.
- Subsequent analyses will focus on sub-segmenting 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)

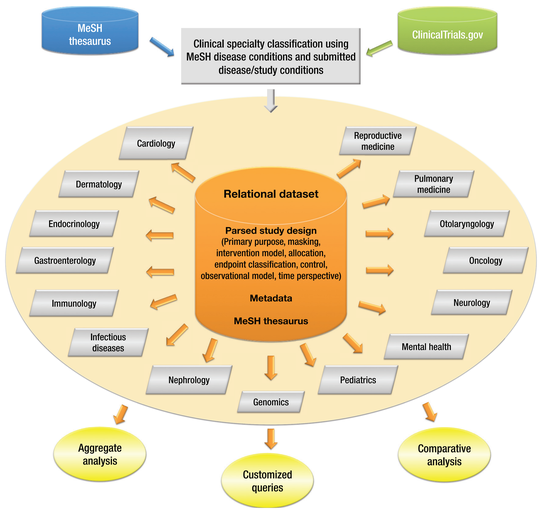

Figure 2 – Cumulative percent of trials in oncology vs. non-oncology by phase

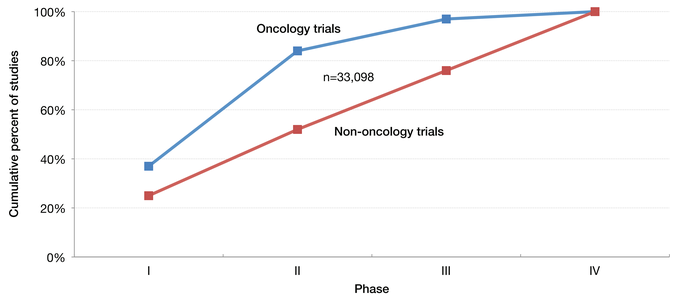

Table 1 – Comparison of oncology and non-oncology trial characteristics

Categories		Oncology (n = 9,040)	Other medicine specialties (n = 29,879)
Intervention model	Single arm	65%	23%
	Parallel	33%	62%
	Crossover/factorial	3%	16%
Masking	Open	88%	47%
	Double blind	9%	40%
	Single blind	3%	13%
Purpose of intervention	Treatment	84%	73%
	Diagnostic	5%	3%
	Prevention	4%	13%
	Supportive care	4%	3%
	Basic science	1%	6%
	Health services	1%	2%
	Screening	1%	1%
Regional distribution*	North America	65%	56%
	Europe	28%	31%
	Asia	16%	15%
	South America	3%	6%
	Middle East	2%	5%
	Africa	1%	3%

* Studies may enroll subjects in more than one region.