Clinical Trials in Nephrology: A Systematic Analysis of ClinicalTrials.gov between 2007-2010

Jula K Inrig, MD, MHS;[1,2] Robert M. Califf, MD;[2] Asba Tasneem, PhD;[2] Radha K. Vegunta, MD;[3] Karen Chiswell, PhD;[2] Uptal D. Patel, MD[2]

[1]Quintiles Global Clinical Research Institute, Morrisville, NC; [2]Duke University, Durham, NC; and [3]University Illinois, Urbana, IL

Introduction

Background:

- Well-designed randomized controlled trials are of paramount importance to improve the delivery of care to patients with kidney disease
- However, it remains unknown whether contemporary trials within nephrology are of the quality and quantity necessary to meet this need
- In 2007, Congress dictated mandatory registration for clinical trials of drugs, biologics, or devices in the US
- As part of a public-private partnership founded by Duke University and the FDA, the Clinical Trials Transformation Initiative (CTTI) developed a high-quality database of registered in clinicaltrials.gov

Objective:

- To describe the characteristics of nephrology trials during the 3 years following mandatory registration and to compare the characteristics of nephrology trials to cardiology trials and to the overall subset of studies

Methods

ClinicalTrials.gov Dataset:

- On 9/27/2010, a dataset of 96,346 studies registered in ClinicalTrials.gov was downloaded. This date was important because it coincided with the 3 year anniversary of the enactment of the FDA Amendment Act of 2007 which legally obligated sponsors to register applicable interventional trials

Nephrology Study Subset:

- This dataset was restricted to 40,970 interventional studies registered between 1/10/2007 and 9/27/2010
- The nephrology dataset was created by using disease-specific condition terms (83 MeSH and 31 non-MeSH) individually reviewed and allocated specific to nephrology (**Supplemental Figure**)
- 1,067 studies deemed specific to nephrology were reviewed by 2 nephrologists to create a final dataset of 1,054 relevant studies
- Similar methods were used to identify cardiology studies

Statistical Analyses:

- Descriptive statistics (frequencies and percentages, median and interquartile range) were used to describe nephrology studies, cardiology studies and the overall subset of studies
- Chi-squared tests were used to compare class variables and Wilcoxon rank sum tests were used to compare continuous variables between nephrology and cardiology
- Statistical analyses were performed using SAS version 9 (SAS Institute)

Results

Trial Design Characteristics:

- Of 40,970 studies, 1,054 were classified as nephrology (2.6%) and 2264 as cardiology (5.5%). Trial characteristics and attributes are demonstrated and illustrated in **Table 1a and 1b** and **Figures 1-3**

Figure 1. Primary Purpose of Clinical Trials within Nephrology

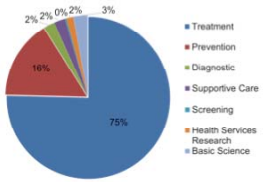


Figure 2. Distribution of Patient Enrollment Targets of Trials within Nephrology

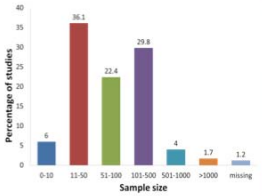


Table 1a. Attributes of Clinical Trials within Nephrology, Cardiology and the Overall Subset in ClinicalTrials.gov

Trial Attribute	Nephrology N=1054	Cardiology N=2264	P-value	Overall* N=40970
Primary Purpose - %			<.0001	
Treatment	75.4%	71.4%		74.9%
Prevention	15.7%	11.5%		10.9%
Diagnostic	2.2%	8.6%		3.9%
Supportive Care	2.2%	2.7%		3.4%
Screening	0.3%	0.5%		0.5%
Health Services	1.4%	2.6%		1.9%
Basic Science	2.8%	2.7%		4.5%
Phase - %			<0.0001	
0	0.3%	0.8%		0.8%
1	8.8%	4.1%		15.2%
1/2	3.7%	2.9%		5.1%
2	16.5%	12.7%		20.7%
2/3	4.2%	3.3%		2.6%
3	16.8%	15.8%		15.1%
4	24.1%	25.6%		13.6%
Not available	25.6%	34.8%		26.9%
Allocation - %			0.26	
Randomized	72.3%	74.1%		68.9%
Non-randomized	27.7%	25.9%		31.1%
Intervention Model - %			0.0003	
Single group	24.9%	26.1%		31.2%
Parallel	64.0%	66.7%		55.9%
Crossover	9.4%	5.4%		11.2%
Factorial	1.8%	1.8%		1.8%
Masking - %			<0.0001	
Open (unblinded)	66.2%	53.3%		55.8%
Single blind	7.6%	15.1%		11.2%
Double blind	26.1%	31.7%		33.1%
Intervention Type - %				
Drug	72.4%	41.9%	<0.0001	60.4%
Procedure	8.6%	15.1%	<0.0001	10.0%
Biological	3.4%	2.7%	0.25	7.2%
Behavioral	3.3%	6.3%	0.0004	8.1%
Device	7.1%	27.9%	<.0001	9.3%
Radiation	0.4%	0.6%	0.38	2.3%
Dietary supplement	3.5%	2.3%	0.036	3.9%
Genetic	0.0%	0.6%	0.013	0.9%
Other	8.3%	12.1%	0.0010	12.5
Enrollment Target – Mean (SD) and Median (IQR)	178 (±621) 68 (30-156)	557 (±2143) 112 (50-300)	<0.0001	450 (±13986) 64 (30-180)

Figures 3a and 3b. Masking Design and Primary Funding Source of Trials within Nephrology

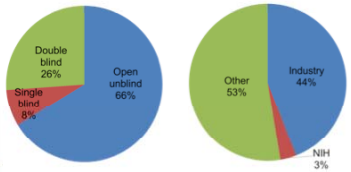


Table 1b. Attributes of Clinical Trials within Nephrology, Cardiology and the Overall Subset in ClinicalTrials.gov

Trial Attribute	Nephrology N=1054	Cardiology N=2264	P-value	Overall N=40970
Endpoint – %			<0.0001	
Safety	6.0%	7.4%		8.9%
Efficacy	33.3%	40.0%		34.1%
Safety/efficacy	49.7%	49.1%		46.4%
Bio-equivalence	1.0%	0.2%		2.9%
Bio-availability	0.3%	0.0%		0.7%
Pharmacokinetics	6.4%	0.8%		3.6%
Pharmacodynamics	1.3%	1.5%		1.4%
Kinetics/dynamics	2.0%	1.0%		1.9%
Missing - (%)	14.0%	17.4%	0.014	19.9%
Has Data Monitoring Committee (DMC)	45.6%	53.0%	0.0002	40.6%
DMC unknown	11.7%	8.6%	0.0047	18.0%
Funding – (%)	(I deleted N row)		0.30	
Industry	44.1%	42.0%		46.0%
NIH	3.3%	4.2%		8.6%
Other	52.6%	53.8%		45.4%
Location - %			0.0077	
US only	37.7%	32.1%		45.5%
Foreign only	56.8%	61.2%		48.0%
Both US & Foreign	5.5%	6.7%		6.5%

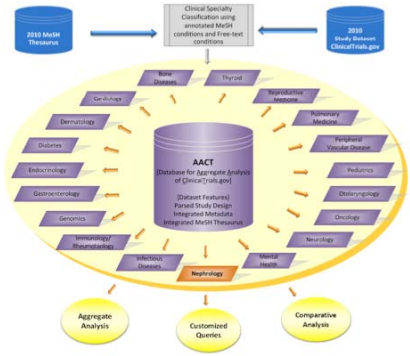
Summary

- In this review of contemporary trends in nephrology clinical trials, we found that nephrology trials comprised 2.6% of studies overall.
- Many trial characteristics were similar between nephrology trials and all others, including those within cardiology.
- However, compared to cardiology, nephrology trials were more likely to have several inferior study design characteristics (such as being unmasked, having small sample sizes, and lacking data monitoring committees).

Conclusion

- Our findings suggest there is significant room for improvement within nephrology to increase the scope, scale, and quality of clinical trials in order to better inform the delivery of more effective therapies for patients with kidney disease

Supplemental Figure. Analysis Methodology



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

Uptal D. Patel, MD
uptal.patel@duke.edu
919-668-8649