Premature Termination of Cancer Clinical Trials: Assessing Trial Efficiency

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INTRODUCTION: Cancer clinical trials fail to reach their planned primary endpoint at a reportedly high rate. Trials which fail prematurely do not contribute maximally to the knowledgebase, if at all, and divert patients from other trials. Optimizing the conduct of cancer clinical trials through improved trial planning, and identifying trials at higher risk of failing to complete, could streamline the trials enterprise and hasten the investigation of new treatments while minimizing patient and investigator burdens. We identified associations with premature termination in genitourinary cancer trials using novel data extraction algorithms.

METHODS: We extracted clinical trial data from ClinicalTrials.gov for prostate, bladder, kidney, testicular, and ureteral cancers. We included only Phase 2-3 interventional trials that had completed or terminated. We designed data extraction algorithms to generate previously unavailable data points for trials, including sponsor and trial information, anticipated and actual accrual numbers (method previously validated and published), and site number and location. We then manually coded reasons for premature termination from the provided free text in the trial record. We considered "toxicity," "adverse events," or "interim analysis" to be appropriate reasons for trial termination as these reasons provide useful information. We identified associations with premature termination via a logistic regression model, with covariates as detailed in Table 1.

RESULTS: A total of 1,106 trials were included. Of these, 298 (26.9%) terminated early, and 249 (22.5%) terminated for a reason other than toxicity/efficacy. The most common reason for termination was poor accrual (46.6%). On multivariable logistic regression, trials with sites outside the USA, prostate or testicular cancer trials, and NIH funded trials were less likely to prematurely terminate. Of trials reported as "completed," 84% met at least 75% of their anticipated accrual goal.

CONCLUSIONS: The rate of premature termination in genitourinary cancer trials is high, with more than 1 in 5 trials terminating prematurely for reasons other than toxicity or efficacy. Interventions are direly needed to optimize clinical trial conduct in order to decrease the drain on patient and investigator resources and hasten much-needed advances in genitourinary cancer care.

Table 1: Associations with Premature Termination for Reasons Unrelated to Toxicity or Efficacy

Variable	OR	95% CI	P value
Anticipated Accrual	1.001	0.999-1.003	
Multicenter Trial	0.82	0.60-1.11	
Site Locations			
International Only	Reference		

USA Only	2.18	1.50-3.19	
Both USA and International	0.44	0.23-0.82	
Sponsor			
Other	Reference		
Industry	0.90	0.64-1.28	
US Government	0.88	0.19-3.15	
NIH	0.56	0.37-0.85	
Cancer Type			
Bladder	Reference		
Kidney	0.72	0.45-1.18	
Penile	0.54	0.03-4.25	
Prostate	0.51	0.33-0.81	
Testicular	0.27	0.06-0.85	