Data driven identification of barriers to accrual in a comprehensive cancer center

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Abstract

Background: Accrual to interventional therapeutic clinical trials is at the heart of any cancer center's research mission. While decreases in accrual noted since 2020 have been attributed to the coronavirus pandemic and limited clinical research staff, underlying structural issues in trial implementation, study availability and diversity, trial populations and trial sponsorship may also be significant yet often overlooked contributors to the overall decline in clinical trial accrual.

Goals: We identified decreases in interventional therapeutic trial accrual over the last 10 years compared to the previous 17 years of analyzed data. We hypothesize that a decreased number of patients accrued per open trial has driven this overall decrease in accrual. Identifying the underlying factors that has led to this decrease in number of patients accrued per trial will focus areas in need of improvement.

Solutions and Methods: We analyzed interventional therapeutic trial data from 1996-2023 at The Ohio State University James Comprehensive Cancer Center. We identified 2236 trials and 24273 interventional therapeutic accruals over this time frame. Information regarding phase of trial, funding source, sponsorship and principal investigators was extracted.

Outcomes: Overall annual therapeutic trial accrual increased annually from <100 annually prior to 1999 to 1663 therapeutic accruals in 2012. The number of new trials opened in any given year as well as the number of trials open for accrual at any given time increased concurrently. After 2012, trial accrual had declined by almost 50% by 2023. However the number of new trial openings and trials open for accrual did not experience a similar decline, instead continuing to increase until pandemic limitations occurred in 2020-2021. When looking at individual clinical trials, the average number of patients put on clinical trial for the span of 1996-2023 was 10.6 pts/trial. This number peaked at 19.6 pts/trial in 2012 and decreased to 6.98 pts/trial in 2023, its lowest value since 1999. Since 1999 the overall breakdown of clinical trials by phase has not significantly changed, approximately 24% Phase I, 7% Phase I/II, 41% phase II, 24% phase III, and 4% other (phase II/III, expanded access, phase IV, compassionate use). Overall accrual by phase was not significantly different over time. When separated by sponsor type, average accrual per trial is highest for externally peer reviewed trials and institutional investigator initiated trials (average 14.7 and 23.7 patients per trial, respectively), while industry sponsored trials have the lowest average accrual per trial (8.1 pts/trial). Prior to 2012, accrual to industry sponsored clinical trials had never exceeded 50% of overall accrual while after 2012 it has never been below 50% of total accrual.

Lessons Learned and Future Directions: The composition of our clinical trial portfolio and accrual patterns based on sponsor type has significantly changed from 1996-2023. Increased reliance on industry sponsored trials has led to lower overall accrual without decreasing overall trial numbers. To counteract this phenomena, we must increase our efficiencies and timelines with industry sponsored trials and expand our portfolio of IITs, externally peer reviewed and national trials.

Background

Accrual to therapeutic interventional trials at academic cancer centers has decreased over the last few years. This trend has been attributed to multiple factors, including the COVID19 pandemic, staffing shortages, lack of quality trials, and competitive slot assignments. We examined interventional therapeutic accruals at The James Comprehensive Cancer Center covering the period form 1996-2023. We noted increasing therapeutic accrual from the period from 1996-2012 while steadily decreasing accruals covering the time-period from 2013-2023. There was no commensurate decrease in the overall number of trials opened each year until 2020-2023, likely commensurate with the COVID19 pandemic and subsequent staffing shortages. Our goals were to understand the landscape of trials and accruals over this time period as a function of phase and sponsor to better define our collective path forward to maximize the appropriate trials for our patients while prioritizing the efficacious use of limited resources.

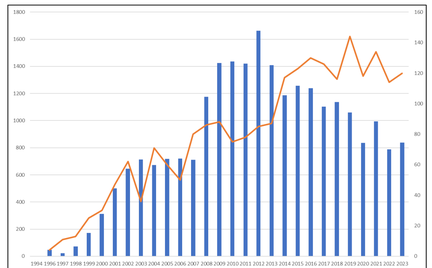


Figure 1. Annual interventional therapeutic accruals (Left Y-Axis, blue bars) and interventional therapeutic trial openings (Right Y-Axis, orange line) from 1996-2023.

Observations

Table 1	
Total Trials	2237
Average time trial open (years)	2.3
Total Investigators	236
Trials opened per investigator	
Mean (SD)	8.9 (13.1)
min, median, max	1, 4, 115

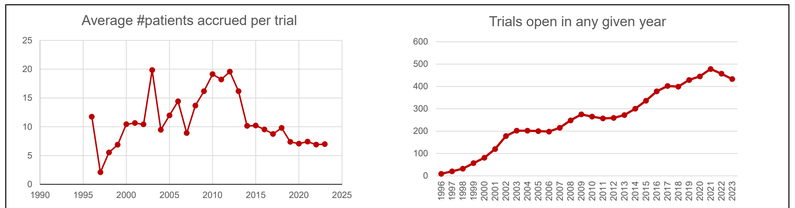
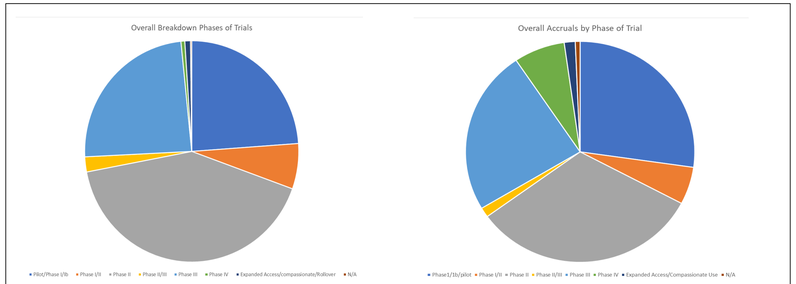
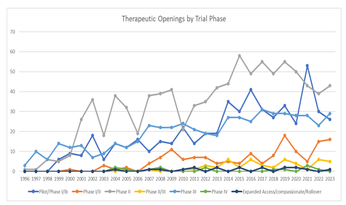


Figure 2. Average number of patients accrued per therapeutic interventional trial based on the year the trial was opened (left) and total number of trials open in any given year (right). This includes all sponsor types and phases of trials.

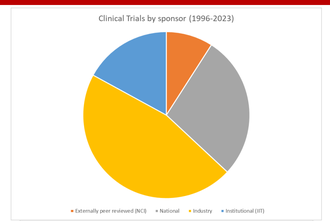




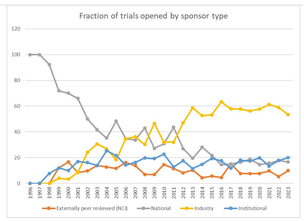
Study Type	Total # Trials	Total Enrollment
Pilot/Phase I/Ib	532	6464
Phase I/II	148	1300
Phase II	926	7666
Phase II/III	49	338
Phase III	539	5716
Phase IV	13	1710
Expanded Access	19	368
N/A	4	161
Totals:	2230	23723

Figure 3. A) Pie chart representation of the overall breakdown of clinical trials opened by the James Cancer center from 1996-2023. B) Accrual to interventional therapeutic trials divided by phase from 1996-2023. C) Annualized therapeutic trial openings by phase

Observations



Average accrual/trial	
Externally peer reviewed (NCI)	14.7
National	10.7
Industry	8.1
Institutional	23.9



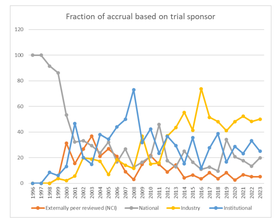


Figure 4. A. Overall breakdown of interventional therapeutic trials by sponsor type from 1996-2023. The fraction of trials opened (B) and accrual (C) as expressed by sponsor type. Externally peer reviewed (NCI) refers to ETCTN and NCI funded multi-center trials; national trials refer to cooperative group (e.g. NRG, ALLIANCE, SWOG, ECOG-ARIN, etc…); Industry trials refer to trials where the IND is held by the industry sponsor; Institutional refers to all trials where the IND is help within the institution independent of funding source.

Lessons Learned and Future Direction

- Noted downtrend in accrual occurred after 2012 independent of the total number of trials being opened
- The fraction of trials opened by phase and accruals to trial by phase have not significantly changed in last 20 years.

Future Directions

1. 2012 was the first year the majority of trials opened were industry sponsored trials and 2013 was the first year that the majority of accruals were to industry sponsored trials. Hypotheses: industry trials are more competitive with less slots available per site.
   - *Possible Future Directions*
     1. *Need to streamline opening and increase total number of industry sponsored trials*
     2. *Select trials with less competitive enrollments*

2. Less institutional/IIT trial opening and accrual
   - *Possible Future Directions*
     1. *Increased institutional support of IITs including TTT working group and funding*

3. More molecularly driven trials limit patient population available for any given trial
   - *Possible Future Directions*
     1. *More comprehensive patient database for trial screening*
     2. *Usage of AI based screening models to better capture patient eligibility*

1. 2010/2014: IOM report on Cooperative group structure followed by dissolution of cooperative groups and new integrated groups (NCTN/NCORP) formed
   - *Possible Future Directions*
     1. *Focus on cooperative group Foundation trials in conjunction with traditional cooperative group trials.*