Closing Time: Protocol Scoring & Remote Closeout for Portfolio Optimization

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Background

Maintaining a heterogeneous portfolio of clinical trials is paramount for a research site to present alternative treatment routes for populations with analogous cancer types who have not responded well to approved treatment options. However, an issue common to many clinical sites is the oversaturation of low-accruing clinical trials. While a promising drug mechanism may seem exciting for patients with a rare mutation at the forefront of activation, slow enrollment in the institution seeking funds to maintain their program has financial ramifications. Further, there is a significant administrative burden in renewing, processing amendments, and providing repeated explanations to internal and external entities for the underperformance of a study. For these reasons, the HICCC has established systems that streamline and amplify trial closures and close-out visit processes to bolster the integrity of clinical trial portfolios across disease teams, offer the most promising investigational agents to our patients, and optimize the financial output of our team efforts.

Goals

- Bolster integrity of clinical trial portfolios.
- Increase rate of close out visit of low/no accrual studies.
- Optimize quality of study start-ups.
- Decrease administrative burden.

Methods

After ramping down research activities due to the COVID-19 pandemic, the Cancer Center needed to define a process for prioritizing start-up studies across the Disease Based Teams (DBTs) portfolios. Statistical analysis of enrollment probability for low accruing studies (Figure 1) was assessed to differentiate which studies would resume and which would be deprioritized. As a result, we developed the prioritization score, which was eventually adapted and incorporated into our feasibility review committee assessment portal.

The Prioritization Scoring review precedes the Feasibility assessment to qualify studies for start-up activities. In Fall of 2020, HICCC deployed the Disease Based Team (DBT) Prioritization scoring process, adapted from an NIH-based scoring system (Andrews, 2013, 5-10), and evaluated during routine DBT meetings. These categories included: scientific merit, clinical need, feasibility, academic output, funding, and resources.

Figure 1. Likelihood of studies with Low/No Accrual to Increase Enrollment Over Time

Subjects Accrued in Year 1	2017-2019 Studies Probability of Accrual in Year 2	2020-2021 Studies Probability of Accrual in Year 2	Change in Probability of Accrual in Year 2
2	16.68 %	7.04 %	- 9.64%
1	4.98 %	2.22 %	- 2.22 %
0	25.89 %	8.75%	- 17.14 %

Post-study activation, the Protocol Monitoring Review Committee (PRMC) annually reviews the predicted study accrual against actual accrual. As of early 2020, studies that do not reach 50% of the anticipated accrual are issued a six-month warning letter by the PRMC. The Principal Investigator is then required to provide a rationale for study continuation.

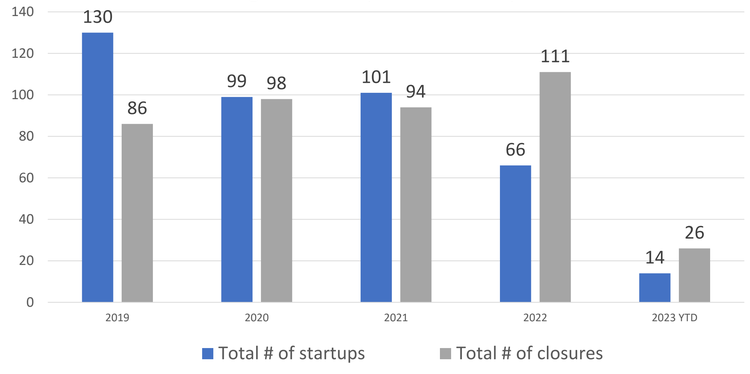
In Fall 2022, the PRMC issued a new initiative to close study enrollment of trials that do not accrue subjects in the first year after study activation. This policy is backed by biostatistical analysis indicating that studies with no accrual or low accrual in the year following activation will not improve enrollment over time (Figure 1).

In tandem with the DBT Prioritization review and PRMC initiative, the regulatory team transitioned to LabArchives, a remote Investigator Site File (ISF) sharing platform. Adopting remote monitoring visits in early 2020 catalyzed the rapid innovation of external monitoring visits. The shift to LabArchives further optimized the secure document review process for our site and monitors by facilitating ISF sharing, external accessibility, and expediting close-out visit review.

Results

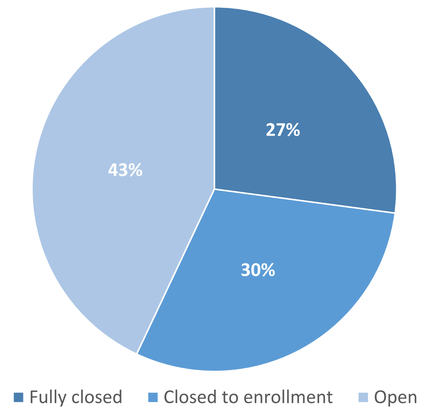
The implementation of the DBT Prioritization Scoring Process has led the investigators to select trials that deliberately satisfy feasibility. The DBT Prioritization Scoring has demonstrated that trials are selected thoughtfully and reduce wasted time and resources, as seen in Figure 2. In the recent year, 2022, the total number of start-ups had reduced by 197% since 2019, when there was no prioritization review, PRMC Warnings, or remote monitoring.

Figure 2. Start-Ups & Closure Comparison



Since enacting the PRMC warning letters, 57% of low-accruing studies have been closed to further enrollment, and about half have been fully closed at our site (Figure 3). Concurrently, utilizing LabArchives for close-out visits has enabled faster scheduling. This platform facilitates remote monitoring visits, and in the recent year, there has been an uptick in closing out studies with poor accruals and inactive studies. In comparison, in 2019, when LabArchives and little to no remote monitoring usage, there was a 77% increase in study closure.

Figure 3. Study Statuses Post PRMC Warnings



Conclusion

The adaptation of the DBT Prioritization Scoring Process has improved the thoughtful selection of start-up trials appropriate for the CUIMC community and within the caliber of the institution. PRMC's initiative of closing underperforming clinical trials has also combatted the oversaturation of low-accruing trials. In combination, the initiatives have reduced administrative burden and, in turn, improved efficiency, quality, and progress toward conducting pivotal cancer clinical trials.

Future Improvements

- LabArchives is being further developed as an eRegulatory platform to eliminate the need for regulatory staff to manually upload documents for external review.
- Optimization of start-up selection during prioritization review is expected to yield increased enrollment in the 2022-2023 period.
- The PRMC reviews studies annually and issues six-month warnings for studies with no accruals. In Fall 2022, PRMC evolved this oversight to close studies with zero accruals after 12 months. PRMC policies will continue to be updated according to the data these policies produce.

Sources:

1. Andrews, Jeff. 2013. “Prioritization Criteria Methodology for Future Research Needs Proposals Within the Effective Health Care Program: PiCMe-Prioritization Criteria Methods” *Methods Future Research Needs Reports,* no. 10 (Jan). 5-10. Available from: https://www.ncbi.nlm.nih.gov/books/NBK116677/

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