Category: Training & Quality Assurance – Completed Project

Risk Based Monitoring as a mechanism to inform DSMC practices

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1. Background

This abstract is a follow-up to the original quality assurance concept presented during the 8th and 9th AACI CRI meetings[1,2]. Based on the need to increase DSMC oversight, and utilizing FDA guidance for Risk Based Monitoring[3], the HICCC DSMC and CPDM Office created study specific data and safety monitoring plans (ssDSMPs) in 2016. Given this process has been in place for 32 months, an evaluation of this process is required in terms of value added to the DSMC Operations Process, and how this RBM approach has improved DSMC reviews. In 2016, there were 21 faculty held INDs and the number has since increased to 34 in 2019. Interventional IITs have grown, and there are currently 54 interventional trials monitored by the HICCC DSMC.

2. Goals

- To evaluate added value of ssDSMPs in the context of DSMC Operations (initial and on-going reviews).

3. Solutions and Methods

Once a ssDSMP is submitted to the DSMC for review, this document is sent to the assigned reviewer to inform the initial trial review from a safety perspective. Completion of the key risk indicators (KRIs) associated with the trial will ultimately determine the trial's final risk score (high, moderate or low risk). More importantly, the DSMC reviewer determines if this information accurately reflects the risk level of the criteria based on the completion of the form, and determines the DSMC monitoring frequency for the trial. This DSMC monitoring frequency dictates the timing of submission of DSMC progress reports (referred to as safety reports), as well as the timing of corresponding monitoring summary forms submitted by the assigned Quality Assurance Monitor. Finally, the monitoring activities defined within the ssDSMP are used as a roadmap for the monitoring summary forms which are submitted to the DSMC for on-going review.

4. Outcomes and Future Directions

The HICCC DSMC has approved 33 ssDSMPs with plans using the updated Risk Based Monitoring Guidance created in 2017. Table 1 includes overall DSMC metrics from January 2017 to April 2019. The implementation of ssDSMPs during initial DSMC review has led to more standardized and informed DSMC reviews. The reviews are now based on pre-determined monitoring risk levels, and reporting frequencies as well as greater integration with quality assurance teams within CUIMC. The DSMC reviewers are able to establish clear guidance for QA monitors at the onset of a trial, and make any required recommendations regarding the ssDSMPs. This has led to a downstream effect of improving the quality of the clinical trials as DSMC reviewers are able to assess the study objectives and safety guidelines (e.g. DLTs) before a trial activates. Finally, the corresponding monitoring summary forms (based on the ssDSMPs) allow the assigned QA monitors to communicate any major findings, and

confirm that monitoring activities are proceeding as planned. During these continuing reviews, the DSMC has an opportunity to address any concerning findings due to this integration. Future directions will include building a comprehensive library of standardized DSMC trainings in collaboration with CPDM Compliance to improve compliance and safety monitoring for the Interventional IITs monitored by the HICCC DSMC.

Figure 1. Type of DSMC review by year

Type of review	2017	2018	2019 (cutoff 4/11/19)
Initial protocol review	9	22	6
On-going safety monitoring	74	91	62
Actionable findings	0	1	1

References:

1. Otap, D, et al. (2016, July). Not the 'Ethics Police', a unique approach to internal Quality Assurance (QA) and monitoring procedures. Poster Presented at the Association of American Cancer Institutes, 8th Annual AACI Clinical Research Initiative Meeting, Chicago, Illinois, USA.

2. Otap, D, et al. (2017, July). Adapting to Thrive- Risk Based Monitoring of Academic Institutional Investigator Initiated Clinical Trials. Poster Presented at the Association of American Cancer Institutes, 9th Annual AACI Clinical Research Initiative Meeting, Chicago, Illinois, USA.

3. FDA Guidance For Industry: Oversight of Clinical Investigations- "A Risk Based Approach To Monitoring, August 2013"1. https://www.fda.gov/downloads/Drugs/Guidances/UCM269919.pdf