Category: Investigator Initiated Trials – Work In Progress

A Risk-Based Approach to Monitoring and Auditing Multicenter Investigator-Initiated Trials

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1. Background

In 2019, the Multicenter (MCT) Office, a team within the Multi-Site Compliance Unit at Memorial Sloan Kettering (MSK), implemented the MSK Clinical Research Quality Assurance risk-based approach to monitoring and auditing multicenter therapeutic investigator initiated trials (IITs). According to the FDA, the risk-based approach ensures quality data by identifying critical data points, which are the most important study elements that need to be reviewed to assess patient safety and a trial's primary and secondary objectives. Data for open to accrual MCT IITs was monitored, while data for closed to accrual MCT IITs was audited.

2. Goals

The MCT team aims to identify the most common deficiencies found during risk-based monitoring and auditing visits for multicenter IITs, as well as the sub-categories of findings within these common deficiencies, to improve workflows and future trainings.

3. Solutions and Methods

To date, the MCT team conducted 26 remote monitoring and auditing visits (22 monitoring; 4 auditing) for 9 MCT IITs. This comprises ~20% of the multicenter portfolio with another ~50% transitioning to the risk-based approach and ~30% following the original quality assurance plan in the protocol. During these visits, critical data points for 86 patients were reviewed and 335 deficiencies were identified.

4. Outcomes

Deficiencies were most common in the following sub-categories:

- General Data Quality (~25%)
- During Study (~20%)
- Protocol Therapy Diaries (~14%)
- Study Treatment/Intervention Administration (~14%)

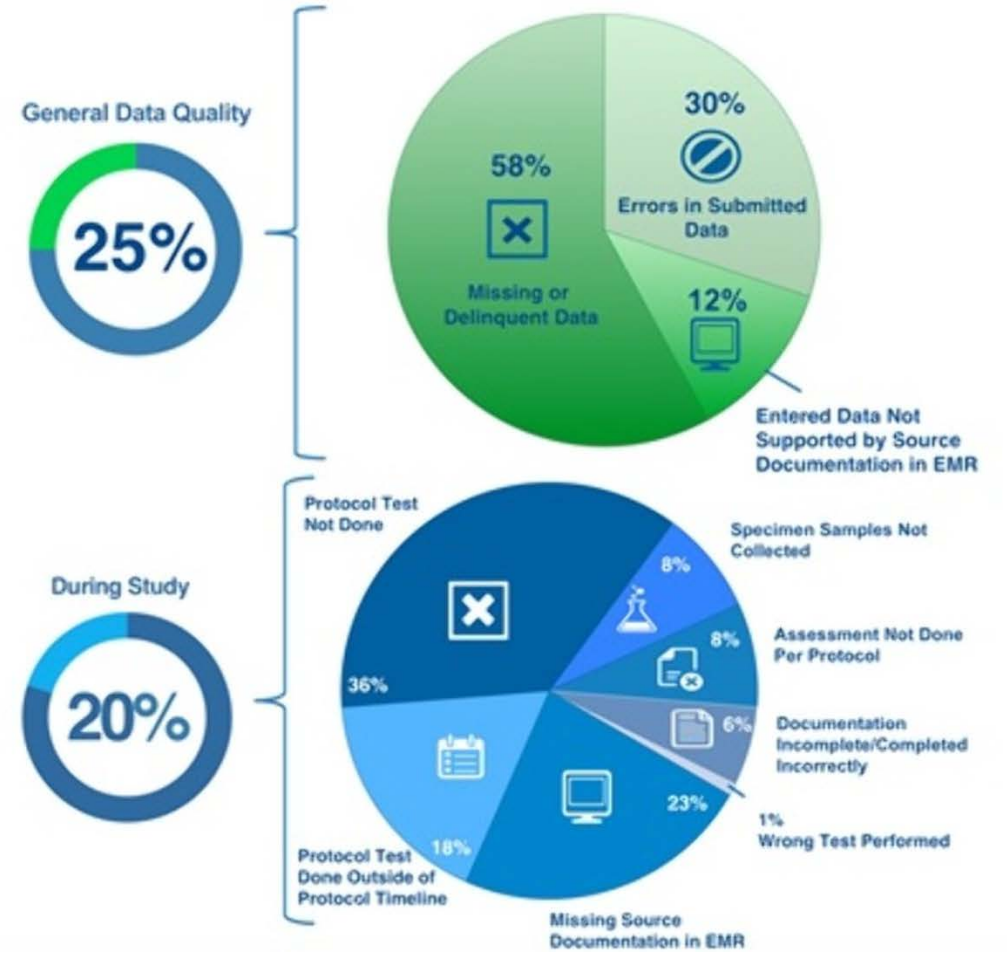
Deficiencies within categories of Eligibility, Toxicity, Regulatory, Baseline, Informed Consent, Treatment Modification, and Outcome/Response were found in frequencies under 10% each.

The most common deficiencies listed above were comprised of the following sub-categories of findings (Figure 1):

- General Data Quality: 58% Missing/Delinquent Data, 30% Errors in Submitted Data, and 12% Entered Data Not Supported by Source Documentation in EMR

- During Study: 36% Protocol Test Not Done, 23% Missing Source Documentation in EMR, 18% Protocol Test Done Outside of Protocol Timeline, 8% Specimen Samples Not Collected, 8% Assessment Not Done Per Protocol, 6% Documentation Incomplete/Completed Incorrectly, and 1% Wrong Test Performed
- Protocol Therapy Diaries: 56% Diary Incomplete or Completed Incorrectly, 32% Intervention Not Administered, 6% Information Recorded Not Contemporaneous, 2% Diary Missing in EMR, 2% Diary Mislabeled, 2% Corrections Not Made Per GCP
- Study Treatment/Intervention Administration: 46% Treatment Administration by Participant Missed; 25% Documentation Incomplete or Completed Incorrectly; 15% Dose Administration Not Documented, 6% Administration by Study Team Missed, 6% Unjustified Delays in Treatment, and 2% Intervention Not Administered

Figure 1



5. Lessons Learned

An analysis of these findings provides insights into current workflows and opportunities for improvement. The MCT team's participation in an Eligibility Verification Program, developed by MSK's CRQA team, likely decreased the number of eligibility deficiencies in 2019. No ineligible patients were enrolled and 7% of total deficiencies were administrative eligibility findings. Going forward, the MCT team will distribute monthly database reports to external participating sites to ensure data is entered in real-time and improve overall General Data Quality. The MCT team will also improve Site Initiation

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Teleconferences and multicenter staff trainings to focus on sub-categories of findings where the most deficiencies were identified, including frequently missed protocol tests and common pill diary errors.