



Importance of Timely Data Submission

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Presentation Objectives

- Illustrate the importance of data submission timeliness
- Communicate the status of Alliance data submission timeliness
- Remind users of tools available to help manage data submission

Importance of Timely Data Submission

- The most important reason we need timely data submission is to protect the well being of our patients!

Data Monitoring Mechanisms

- Safety Monitoring
 - Adverse events
 - SAE
 - AE rate
- Efficacy Monitoring
 - Interim analyses
- Routine Reporting
 - NCI via CDUS reporting (quarterly), DSMB (biannual), CIRB (yearly)
- Data Reviews
 - Eligibility
 - Case evaluations

Monitoring

- Data Safety and Monitoring Board (DSMB)
 - Meets biannual to review the safety and efficacy of trial data and makes recommendations about the timing of trial closure and release of study data to the sponsor and public
 - In order to review safety and efficacy data, data needs to be relatively complete
 - There are inherent biases in the rate data comes in
 - Example, events (deaths) are typically reported more quickly than non events, thus if data is not complete decisions may be impacted

Safety Monitoring

AE Stopping rules

- Alliance trials include Adverse Event stopping rules
 - Example from A091302: If at any time, 3 of the initial 10 treated patients or 30% or more of all patients (i.e. when accrual is greater than 10 patients) have experienced a grade 4 adverse event.
- To assess whether an AE stopping rule has or has not been met, timely AE data is needed

Safety Monitoring

- CTEP-AERs – Rave Integration
 - The main goal of the integration is to synchronize the safety and routine AE databases and provide a recommendation about whether an AE does or does not need to be reported in an expedited fashion
 - In order to provide the recommendation, the key elements of an AE need to be entered in real time
 - If a site is behind on their data entry and they want to report an SAE, they will need to roll out folders to get to the current cycle of treatment

Routine Reporting

- Clinical Data Update System (CDUS)
 - CDUS reporting is the primary resource of clinical trial data for the NCI to fulfill their regulatory, scientific and administrative needs.
 - For NCI's monitoring to be meaningful, data needs to be complete and accurate
 - Submitted quarterly and all identified errors must be resolved for the report to be accepted
 - Example of an error: If an AE is reported on a cycle and there is no treatment information corresponding to that cycle

Central Monitoring

- Required by NCI for all trials where CTEP holds the IND
- Source documentation is submitted so that a central monitor can verify key trial data in real time
- Key trial data
 - Eligibility, first 2 cycles of treatment, off treatment, endpoints

Data Reviews in Real time

- Main goal to identify and correct any data issues quickly and before errors are repeated in subsequent cycles and future patients

Eligibility Review

- Eligibility reviews are conducted in real time by Data Managers and Study Chairs
- Data Managers are flagged to perform an eligibility review when all required forms and source documentation are entered within Rave
- Eligibility reviews done in real time
 - Allows study teams to identify areas of the eligibility criteria that are confusing or require further education before trials are negatively impacted by high rates of ineligibility

Case Evaluations

- Case Evaluations are conducted in real time by Data Managers and Study Chairs
- Data Managers are flagged to perform a case evaluation when a trial endpoint has been reported in Rave
 - Progression, death, lost to follow-up, withdrawal of consent, follow-up completed
- Case evaluations done in real time
 - Allows study teams to identify issues with data collection or endpoint determination that can then be corrected before having negative impact on trial outcomes

Efficacy Monitoring

- Interim analyses are pre-specified in the protocol and often occur when a given number of events (such as progression) have been reported
- For fast accruing trials it is especially important to receive timely data submission so an interim analysis evaluating endpoint data can be conducted before accrual goals have been met

Trial Examples

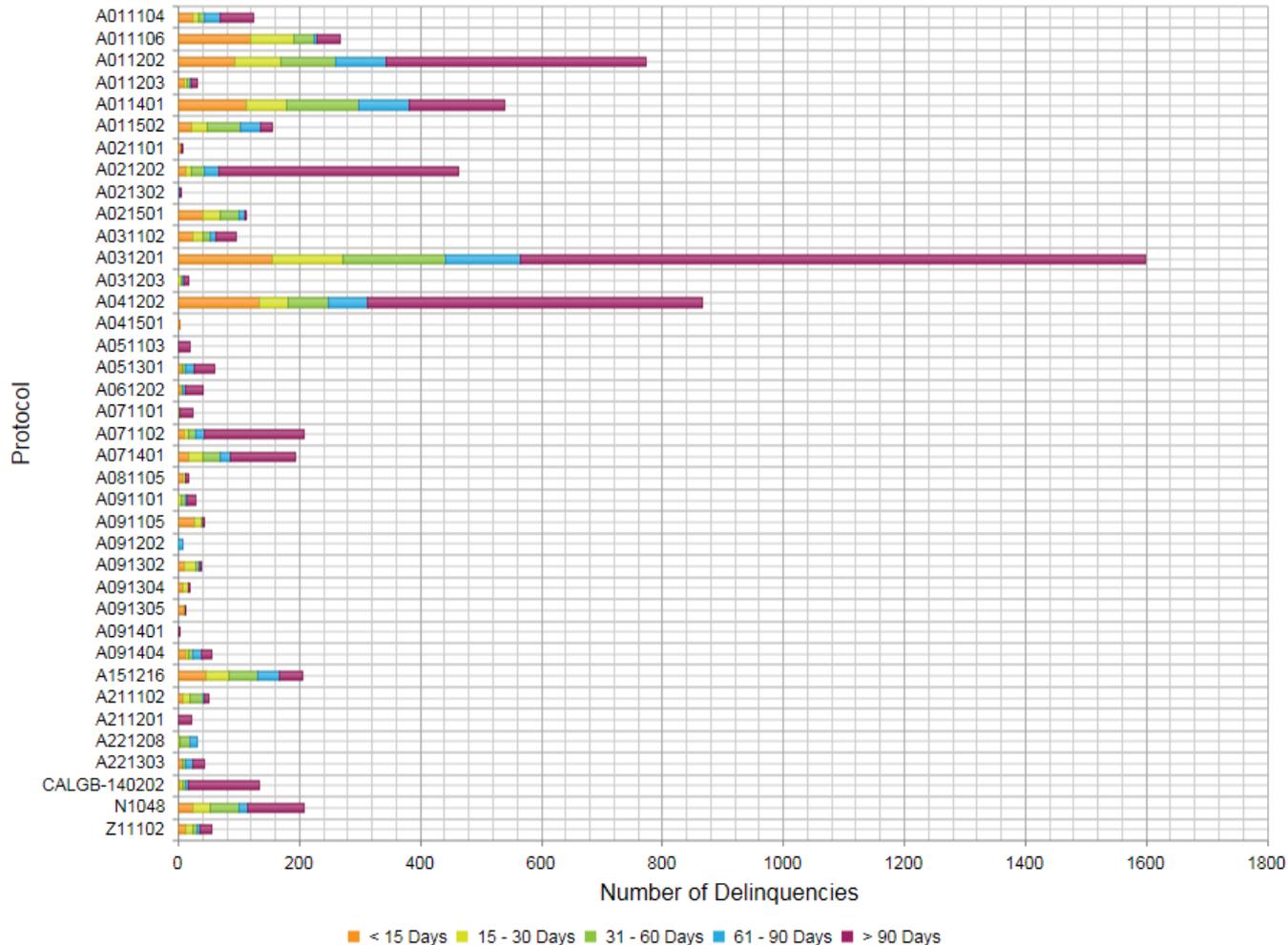
- Trial A021501:
 - Rapid accrual
 - There is a choice between Stereotactic Body Radiation Therapy (SBRT) and Hypofractionated image guided radiation therapy (HIGRT) but it is critical to the trial results to ensure a large % of pts receive SBRT
 - Concern: Completing enrollment only to find when data is received that the needed % of SBRT pts was not met

Trial Examples

- Trial A021202:
 - Patients go off treatment based on central review of recurrence
 - Since treatment is impacted based on review it is critical for data to be entered in real time to support the central review of recurrence

Alliance Data Timeliness

Delinquency Aging Report Summary for LPO ALLIANCE



Alliance Data Timeliness

- Institutional Performance Evaluation Committee (IPEC)
- A number of Alliance sites are at risk for probation at the next group meeting for having their third consecutive evaluation with a -2 score in data submission timeliness
 - < 75% of data submitted on time

Alliance Data Timeliness

- There are tools to help!
- Overdue Material Reports on the Alliance website
- Data Quality Portal on the CTSU website
 - Note: Data submission timeliness data is now available to NCI across all cooperative groups
- Rave Task Summary

Overdue Material Tracking

- Do **NOT** respond to queries about missing data by indicating “pending” or “cycle not complete”
- The query is a reminder that data is still needed

Take Home Message

- Timely Data submission is critical to the success of the Alliance reasons including:
 - Safety and efficacy monitoring to protect our patients
 - DSMB, CDUS, CIRB reporting to fulfill regulatory requirements
 - Eligibility and case eval reviews to identify potential data issues and correct them as quickly as possible
- The Alliance needs to improve its data submission timeliness
- There are tools to help