PINTAD

The Pharma Imaging Network for Therapeutics and Diagnostics

Meeting Minutes

Topic	Imaging in Clinical Trials Despite COVID-19
Date	30-October-2020
Speaker(s)	Brenda Kurland, Fabien Ricard, Greg Goldmacher

Slide	**Discussion**
Welcome (*Brenda Kurland*)	Wanted to bring everyone together since everyone is having different experiences. Discuss what people are doing, and long-term impacts.
Slide 1 - Slide 10 (*Fabien Ricard*)	FDA guidance on COVID-19 https://www.fda.gov/media/136238/download https://www.fda.gov/media/137290/download
Slide 11 – Slide 14 (*Greg Goldmacher*)	Overall survival has huge limitations, so we must get imaging done. How can we deal with handling the loss of some imaging, and minimize the impact on the data?
Discussion	*Dave Raunig* – there are 5 strategies that the FDA allows to adjust for COVID-19. If timepoints are missed then an event is observed, interval censoring should be accounted for by established methods (see work of Michael Fay, including PMID25285054). Competing risks are another analysis approach relevant to time-to-event endpoints. The FDA has made it clear that the desired target of inference is treatment effects in the absence of COVID-19, but appears to accept only "as treated" analysis rather than principal stratification (causal analysis estimating effects under the counterfactual of "no COVID-19 impact"). Dave to send reference literature. **Question:** Should protocols be updated to reflect these changes? **Discussion**: • *Greg Goldmacher:* Has not changed assessment schedule. They are assessing impact on missing data and flagging the missing data. • *Dave Raunig*: Also, not changing the protocol but will need to update the SAP before the database lock. **Question:** Kelie Luby: From a patient perspective, they may want to go to a site closer to them. It can be very difficult for a patient to get their scans from one facility to another. What kind of guidance can we give to patients and the investigators for moving the images? Ambra makes scans more portable. **Discussion**: • *Greg Goldmacher*: The issue with Ambra is that not everyone will have it. • *Kelie Luby*: Even treatments are being delayed because the investigator site is waiting to get the patient's scans. We should think about how/where some of this information/guidance can go (protocol, site imaging manual).

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	• *Greg Goldmacher*: A radiology report will at least allow the investigator site to make treatment decisions. • *Brenda Kurland*: Instruct patient to get 2 copies of their scans on CD • *Guenther Brueggenwerth:* In the good old days we would just send the CDs by DHL. You would have to get the form/pre-paid airbills to the patient or the site. [some sites without capacity for internet upload still do this] • *Dave Raunig:* If you think of all radiologists as exchangeable (data supports this) you could move the read to be just a single central reader. • *Greg Goldmacher to Guenther Brueggenwerth:* Have you actually implemented the pre-paid air bills? • *Guenther:* No. We haven't had to change our operational processes yet. **Discussion:** What are others in the industry doing? • *Terri Binder*: Doing the same kinds of things that Merck is doing, but so far there have not been large amounts of missing imaging. They are doing sensitivity analysis, and not just censoring patients in the traditional way. If a patient is getting imaging off-site, it is very important to get the images to the investigator so they can make an assessment. The investigator should assess them, not other radiologists. • *Ira Smalberg*: From March-April there may have been a 20% dip in images coming in (20% of scans were missing), but that did improve again. • *Matthew Marini*: Some of those missing images were missing because site personnel could not get into the facility to access the images, and they were able to send them when the lockdown lifted. The question is, how many of the scans were not delayed or not performed, vs. delays in site or central reads. • *Paul McCracken*: On a daily basis ICON generates reports on query trends and missing data vs. expected. The number was up around 6% in August. Based on the most recent data he has, he has seen a minimum of 2% of sites had a COVID-related query response, but he believes it is now creeping back up to around 4%. • *Peter Steiger*: His experience has been similar to the others who have shared. Big decrease in March and April but it has rebounded. Overall, sites and organizations have found a way to continue to gather and organize data. **Additional Points and Questions:** • Some patients are afraid to go get scans, depending on their disease status (e.g. adjuvant).

Slide	Discussion

	• Consensus: Patients to get 2 copies of their scans, and put one CD into the pre-paid air-bill to the site.
	• *Ninad Mantri*: How are others forecasting endpoint driven analyses given the missing data.
	  ○ *Greg Goldmacher*: if the central read has already given you your event, you can accept that.
	• *Jarrod Klayman*: Do we anticipate that COVID-19 might become part of inclusion/exclusion criteria?
	  ○ *Greg Goldmacher:* Hasn't seen anything directly, but certainly decreased function (pulmonary or otherwise) may exclude them.

Close out (*Brenda Kurland*)	The pandemic is unprecedented, but these issues are not. With clear heads we can tackle these issues. Communication with sites, staff, patients is difficult with so many at home with young children. Be kind. Thank you for participating. Next Session: December 11th (Non-Oncology Topic)