

Pharma Imaging Network for Therapeutics and Diagnostics (PINTAD)

MEETING SUMMARY

MEETING SUBJECT:	PINTAD 2013 Telecon
DATE / TIME:	27SEP13 / 11:00 AM EST
PREPARED BY:	Barbara Chandler, Annette Schmid
LOCATION:	Teleconference

DISCUSSION POINTS:

1	<p>Q & A with Dr. Lori Dodd (LD) and Dr. Ohad Amit (OA) on their thoughts and suggestions on the implementation of the Audit Methodology</p> <p>1. Would an electronic data capture system be required at the site level to enter responses are case report forms adequate? Would this data need to be 100% source data verification before it can be evaluated in an audit setting? Could the same report being used at the site for patient management be considered a source document for the audit or would a separate report need to be generated?</p> <p>OA: the more electronic the better, mostly all electronic now anyway</p> <p>2. Is there a need to train/qualify site readers as well as ensure the same reader evaluates each time point from an individual patient? Would these site radiologists need to complete a 1572 and Financial Disclosure since they will likely request payment as their site reads are now directly part of the clinical trial?</p> <p>LD: At FDA Advisory meeting they debated this in regard to reducing measurement variability as much as possible. It may not be feasible in large Phase 3 trials.</p> <p>OA: Try to standardize the process to reduce noise. The quality is acceptable now. The process is not broken.</p> <p>LD: It depends on the disease indication. The meta-analysis showed the investigators do a reasonable job. It doesn't mean we can't get better. Encourage quantitative assessments in the future. Reader variability is an important issue.</p> <p>3. Is this approach more acceptable for a particular type or phase of clinical trial? For example: is adjuvant setting ideal? Should this focus on just Phase 1, 2 or 4 but not pivotal Phase 3? How would a trial that includes the need for clinical evaluation by an oncologist be implemented ie. for Melanoma or Lymphoma?</p> <p>OA: Phase 3 is where you want to do this with a PFS endpoint. Response rate may be different. In a Phase 2 study you're looking for a signal corresponding to drug treatment. The site review is sufficient. A Phase 4 study may depend on regulatory considerations. Can't talk about lymphoma. For melanoma include photographs with scans. It's not unreasonable for the radiologist to review photographs.</p> <p>LD: Disagree about the need for independent review if Phase 2 trials since there's more risk and more tendency for reader bias. There was a prostate trial that used the audit method where 20% of</p>
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	<p>PD events were read and this was submitted to FDA.</p> <p>OA: Aware of it but it did not have a PD endpoint. Phase 2 audit is not very useful due to sample size and the cost/benefit argument.</p> <p>4. How would the gold standard be established? Would it be based on the evaluation of site data by a single central reader? If the reader does not agree with the site, would there be need for adjudication?</p> <p>LD: Proceed to a full central review. If there's till discordance, that's an interesting question.</p> <p>OA: Same</p> <p>5. What should be the focus of the thresholds for determining acceptable site reads? Would it be based on the clinical outcome at the end of the study to be most accurate?</p> <p>OA: Have all scans centrally managed to minimize delay. Majority of times or 9 out 10 you're not going to have to go to full read.</p> <p>Question about retrospective scans. OA: Design audit prospectively in the protocol. Define what is the threshold for success and what will trigger a full review. That's the biggest point of disagreement.</p> <p>LD: Real time reviews are the solution to issues about informative censoring. Our method does not address it, the only thing that does is real time review.</p> <p>OA: There's more work to be done. FDA is jumping ahead. I know sponsors moving ahead with our method. Confirmation of PD was proposed. Lori was on the RECIST committee and they declined to include this.</p> <p>LD: (in response to comment about site reads being influenced by personnel) Even with that taking place, it doesn't seem to have an effect. Meta-analyses are important.</p> <p>Lori and Ohad agreed to meet at another time to continue the discussion.</p>
2	<p>Next meeting 25OCT2013, 11:00 AM EST</p> <p>Update on Site Investigator perspective on audit methodology</p>