PINTAD

The Pharma Imaging Network for Therapeutics and Diagnostics

Meeting Minutes

Topic	**Tumor growth modeling in drug development: tool for early phase decision and assessment of response to therapy**
Date	26 March 2021
Speaker(s)	**Antonio T. Fojo MD**. Dr Fojo is Professor of Medicine at Columbia University and Medical Oncologist at the James J. Peters VA Medical Center. His basic research interests include microtubule targeting agents and how they interdict intra-cellular trafficking in cancer cells, and the development of therapies for neuroendocrine and adrenocortical cancers. Clinically he conducts translational research with a focus on adrenocortical cancers, pheochromocytomas / paragangliomas, neuroendocrine tumors and prostate cancer. Finally, he has an interest in novel clinical trial endpoints, with a special interest in what clinical trial data tells us about the basic biology of cancer.

Topic/Slide	Discussion
Summary	Tumors grow and regress exponentially Efficient use of volumetrics and modeling would allow smaller clinical trials compared to those with common endpoints (RECIST)
New software	Physician facing and patient facing results, including population comparisons
Discussion	*Greg Goldmacher*: People have tried to do this with RECIST before, without much success. Requires identifying ALL lesions present. *Antonio T. Fojo*: Can use RECIST data, but it would be better to collect volumetric data; modeling accommodates different intervals between imaging timepoints. *Larry Schwartz*: Initial data suggests – is it more lesions, is it volumetric, or both? AI improvements will mitigate these issues. When RECIST was used, it was negligible (more lesions/volumes). We will need more consistent collection of volumetric data. *Dave Raunig*: Longest diameters demonstrated reduced radiological burden 30 years ago. With advances in technology, we can now rely on AI to measure volumes easily. Because diameters are lognormally distributed, simply adding longest diameters is a suboptimal measure of tumor burden. *Antonio T. Fojo*: The data is meant to show “superiority” instead of “not inferior.” *Larry Schwartz*: Future effort look to get regulatory guidance and acceptance from FDA and working with PINTAD on gaining acceptance – making standard practice.

Topic/Slide	Discussion
	Dave Raunig: Might want to consider Bayesian scheme where you fix g and let theta vary over time – there has been some acceptance from the FDA using a Bayesian scheme *Ned Uber*: How do you handle inflammation/tissue changes unrelated to disease. *Antonio T. Fojo*: You can't control for that. *Greg Goldmacher*: Could consider using CT textural analysis. *Larry Schwartz*: Takes longer to analyze the images, but who cares if its 30 patients instead of 1200 patients in a trial. *Ned Uber*: Matters if recommended for clinical practice.
Close Out	PINTAD to organize a follow-up Meeting
Meeting Chat	[11:25 AM] Raunig, Dave Wouldn't the log of the g-value always be linearly correlated to the MOS when using an exponential survival function? [11:25 AM] Raunig, Dave What happens when the survival function is Weibull or Lognormal? [11:28 AM] Raunig, Dave Could a multiple model that weights by the likelihood of the model be used to determine the shift, if there is a shift, to progression from regression and then use that point to define date of progression. See Bar-Shalom and Li 1993. The problem is that the HR is fairly robust to noise in the data, remarkably enough pointed out in a Dodd paper (Sridhara, Mandrekar, & Dodd, Clin Cancer Res 2013). [11:34 AM] Raunig, Dave The real contribution of this model is the first-principles link to OS that is sorely missing for RECIST PFS. [11:42 AM] Raunig, Dave Instead of a fixed theta, theta could be a function of time and be based on likelihood function of the terms. which is a very elegant Bayesian schema. [11:51 AM] Majmundar, Vrajesh (Guest) Robust consistent image isotropic data acquisition needed for volumetric analysis

Topic/Slide	Discussion
	[11:51 AM] Ned Uber what about immediate inflammation response. Metabolism better???