gain-of-function model, TGM2 was upregulated in HMLE-E2 cells and compared to shTGM2 knockdown BM cells. Growth rates were analyzed using metabolic activity over 8 days, and drug sensitivity to Neratinib (0-1000 nM) was analyzed via cell titer. To account for the different transport properties of the 3 distinct culture environments, we developed a mathematical model for each condition, allowing us to normalize the drug sensitivity results across models to effectively compare true biological resistivity. RESULTS/ANTICIPATED RESULTS: We observed that increased cellular levels of TGM2 significantly increase the growth rate and drug resistivity of cells on fibronectin matrices. Interestingly, in 2D cultures, TGM2 expression was correlated with higher Neratinib resistivity but did not affect growth rates. In spheroid models without a significant matrix component, that rely solely on cell-cell junctions, high levels of TGM2 were correlated with lower survival rates. Lower levels of TGM2 are correlated with a more epithelial phenotype, and using our mathematical model we have identified significant transport differences between high and low TGM2 spheroids. We theorize that the low TGM2 spheroids have denser packing, which lowers the rate of diffusion and, thus reduces the effective concentration of the drug to the majority of the cells. DISCUSSION/SIGNIFICANCE OF IMPACT: Our studies indicate that the cellular response to drugs can be altered by changes in both transport properties of the tissue and the CM interactions. By systematically investigating the effects of CC interactions and CM interactions, we can use mathematical models to delineate physical means of drug resistivity from a biologically driven resistance.

Regulatory Science

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Implementation of Real-World Data and Real-World Evidence in Clinical Studies

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OBJECTIVES/GOALS: Real-world studies have been gaining momentum in providing evidence of treatment effectiveness and hold great potential for facilitating the drug regulatory process. The U.S. Food and Drug Administration (FDA) has recognized this by providing a framework for using real-world data (RWD) to generate real-world evidence (RWE). The objective of this study is to assess the current level of RWE implementation in clinical studies. METHODS/STUDY POPULATION: Using keywords relevant to RWE, we reviewed studies on drugs, biologics, and medical devices published on PubMed in 2018. Information regarding the therapeutic area of focus, intervention type, study design, primary outcome, and data source was recorded. Further analyses of the three main therapeutic areas of study (oncology, cardiology, and infectious diseases) were performed to determine how RWE was being utilized. In addition, a broad "real-world" search was performed on Clinicaltrials.gov, from which we extracted relevant observational and Phase I, II, II/III, III, III/IV, and IV studies. A supplemental PubMed search was used to evaluate published studies in order to identify which field these trials were concentrated in and the outcome of interest." RESULTS/ANTICIPATED RESULTS: After application of "real-world" search terms to PubMed, 995 hits were generated and of these, 311 studies were excluded. More than half of the studies were observational and retrospective in nature (64%) with 70% examining drug/biologic outcomes. RWE data sources were largely dominated by medical records and claims data. The primary uses of RWE across oncology, cardiology, and infectious diseases included supporting drug product effectiveness, assessing safety, and evaluating treatment patterns. Of the 207 RWE studies identified on ClinicalTrials.gov, 66 were cancer randomized controlled trials (RCTs), a majority of which were used for post-marketing safety evaluations. Further research will be conducted to determine the precise role of RWE in all studies (e.g. historical comparator, label expansion). DISCUSSION/SIGNIFICANCE OF IMPACT: By examining the use of RWE in regulatory decision making, we can inform stakeholders of the extent to which robust RWE studies complement evidence generated by RCTs. Thought to reflect a product's performance in a broader and more diverse population, RWE can provide greater insight to clinical trial conduct and ultimately transform patient outcomes.

4500

Providing a System for Practical Monitoring Training for Clinical Trials within Academic Institutions

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OBJECTIVES/GOALS: The goal was to understand the effectiveness of a novel clinical trial educational module and a corresponding initiative designed and disseminated by the Southern California Clinical and Translational Science Institute (SC-CTSI) to increase the quality of clinical trials conducted in academia. METHODS/STUDY POPULATION: The CRCs (Clinical Research Coordinators) for the initiative are asked to complete the online training. Possible study protocols are picked to be monitored by the CRCs. The monitor is instructed to study the protocol extensively and prepare for their monitoring visit. The trained monitor from the initiative then reaches out to the CRC of the study that is to be monitored and carries out the monitoring visit. Afterwards, the monitor sends initiative personnel the monitoring report, which is evaluated to see if the monitor checked everything they should have during the visit. The PI of the study is contacted with highlights from the monitoring report and improvements that they can make. RESULTS/ANTICIPATED RESULTS: The first study monitored was a site of a large NIH-sponsored study where the consent forms were signed electronically. It was found that the monitor could not access the consent forms. Therefore, the monitor could not do source data verification. The PI of the study said that they would be raising this issue with the NIH. During the monitoring visit of the second study chosen for the initiative, patient binders were specifically examined for informed consent and source documentation completeness. The charts of patients were also reviewed. The only deviation found was a missing signature in the Investigator Site File. For the last two studies, data will be reported. DISCUSSION/SIGNIFICANCE OF IMPACT: Monitors were not only able to monitor efficiently, but also able to point out deficiencies in the monitoring practices of large studies. This model could be expanded to other academic institutions to

https://doi.org/10.1017/cts.2020.347 Published online by Cambridge University Press