of CT infection is distinct from women with persisting chlamydia. These studies may inform whether IFN-γ, produced by CD4+ T-cells, or tryptophan-dependent or -independent metabolic pathways are associated with natural clearance, which may advance chlamydia vaccine development.

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Serial Biomarker Monitoring Predicts Long Term Outcomes in Acute Graft Versus Host Disease

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OBJECTIVES/SPECIFIC AIMS: The first aim of the study is to evaluate the accuracy of serum biomarkers of acute GVHD measured after four weeks of corticosteroid therapy to predict 6 month NRM. The second aim of this study is to compare the accuracy of the biomarker algorithm to that of clinical response to corticosteroids after four weeks. The third aim of the study is to develop a novel regression model that uses weekly biomarker measurements over the first month of corticosteroid therapy to predict 6 month NRM. METHODS/STUDY POPULATION:. Patients who received HCT at one of 22 IRB-approved centers and provided blood samples to the Mount Sinai Acute GVHD International Consortium (MAGIC) biorepository and developed GVHD between January 2008 to May 2018 are included in this study. Patients were divided by time into a training set (Jan 2008-Dec 2015, n=233) for model development and a validation set (Jan 2015-May 2018, n=357) to evaluate the predictive performance of the model. The later time of the validation set was chosen deliberately to model contemporaneous GVHD treatment practices. The size of each group was designed so that there would be roughly equal numbers of deaths in both groups. RESULTS/ANTICIPATED RESULTS:. Serum concentrations of GVHD biomarkers after one month of corticosteroid therapy were measured in the validation set, and the predicted probability of NRM ($\hat{p}$) was computed according to the previously published algorithm: $\log[-\log(1 - \hat{p})] = -11.263 + 1.844(\log ST2) + 0.577(\log REG3\alpha)$. The performance of the biomarker algorithm was evaluated by creating receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC) in the validation set. The AUC of the biomarker algorithm was a significantly better predictor of 6 month NRM than clinical response to treatment after four weeks of corticosteroids (0.84 vs. 0.64, $p<0.001$), which is a clinically relevant improvement in accuracy. To evaluate serial biomarker monitoring, serum biomarker concentrations will be measured weekly at five time points from treatment initiation to one month after corticosteroid therapy. We will use these values in the training set to develop a regression model for 6 month NRM that accounts for repeated biomarker measurements. The performance of this model will be tested in the validation set and the accuracy of the serial biomarker measurements will be compared to the accuracy of measuring biomarkers at the single time point after four weeks of corticosteroid therapy. An AUC improvement of 0.05 would be considered clinically significant. DISCUSSION/SIGNIFICANCE OF IMPACT: Clinical response to treatment after four weeks has been the standard endpoint in GVHD interventional trials for decades. If biomarkers measured at the same time more accurately predict long term mortality, this study would provide the basis for a novel endpoint in GVHD trials and enable more accurate determination of effect size of experimental interventions. An accurate biomarker algorithm will prove useful in guiding immunosuppressive treatment decisions for patients with GVHD. Patients identified by the algorithm as low-risk may benefit from reduced-dose corticosteroid therapy, potentially reducing lethal opportunistic infections. Patients identified as high-risk will be candidates for more intensive immunosuppression or investigational therapies. This precision medicine approach tailors therapy to the individual patient's biology.

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Sunitinib-Induced Cardiotoxicity in an Engineered Cardiac Microtissue Model

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OBJECTIVES/SPECIFIC AIMS: The aims of this study are threefold. Firstly, we are examining the effects of increased in vitro afterload (a proxy for hypertension) on human induced pluripotent stem cell cardiomyocyte (hiPSC-CM) response to sunitinib in a durable and dynamic cardiac microtissue culture system. Secondly, we are exploring effects of repeat exposure and recovery of both sunitinib and afterload throughout the lifetime of the hiPSC-CM microtissue. Finally, we are assessing methods to prevent and treat sunitinib induced cardiotoxicity. Primary outcomes for this study are commonly utilized metrics of cardiotoxicity: degree of caspase activation, electrophysiology benchmarks for minimum voltage threshold and maximum capture rate, and microtissue force generation. METHODS/STUDY POPULATION: HiPSC-CMs are cultured and matured as 3D cardiac microtissues (CMTs) on a microtissue array. After maturation, cells are exposed to sunitinib doses of 0μM, 0.5μM, 1μM or 5μM for 12 hours. Concurrently with sunitinib dosing, increases in microtissue array stiffness are created with application of an external magnetic field. Afterload spring constants are fixed at pre-determined physiologic values ranging from 0.5μN/μm, to 5μN/μm. For Aim 1: Half of the CMTs are harvested at 8 hours after sunitinib dosing to conduct the caspase 3/7 assay, and the remainder are examined for 3 days following drug exposure to track temporal changes in electrophysiology and force generation. For Aim 2: After CMT maturation, 12-hour exposures to sunitinib are repeated three times at a fixed dose, with doses separated by one week. Concurrently with sunitinib dosing, increases or decreases in microtissue stiffness are created by changing the strength of an applied external magnetic field to create "ramp up" or "ramp down" stiffness conditions. Caspase assay and contractility metrics are measured at each timepoint. For Aim 3: Experimental conditions are conducted as described in Aim 1. Prior to the introduction of sunitinib, either carvedilol or an AMP-kinase activator is added to the CMT culture media at physiologic concentrations. Primary outcomes are examined as in Aim 1. RESULTS/ANTICIPATED RESULTS: Aim 1: We hypothesize that increases in microtissue afterload, synchronized with sunitinib exposure will augment sunitinib toxicity in cardiomyocytes resulting in elevations of caspase 3/7 activity and minimum voltage capture as well as decreases in maximum capture rate and maximum force generation. Aim 2: We hypothesize that repeat

https://doi.org/10.1017/cts.2019.261 Published online by Cambridge University Press