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### A Phase I Trial of Tazemetostat and Venetoclax in Relapsed and Refractory non-Hodgkin Lymphoma

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**OBJECTIVES/GOALS:** Primary Objective: To evaluate the safety of venetoclax plus tazemetostat in patients with relapsed and refractory (R/R) Follicular lymphoma (FL) or Diffuse large B-cell lymphoma (DLBCL) Secondary Objectives: 1. To evaluate the tolerability of the combination of T+V using patient reported outcomes (PROs) 2. To evaluate the efficacy of T+V **METHODS/STUDY POPULATION:** Study design: A phase I trial in two parts: Part 1: a single-arm, open-label sequential dose escalation (3+3) of venetoclax in combination with tazemetostat, given at its recommended phase II dose (RP2D) of 800mg BID, to determine the maximum tolerated dose (MTD) of venetoclax. Part 2: two expansion cohorts (R/R DLBCL and R/R FL) to further characterize the safety and tolerability of the combination, and to estimate the preliminary efficacy. We will perform additional exploratory studies to determine if there are biologic features that correlate with responses. Eligibility: up to 38 patients aged  $\geq 18$  years old with histologically confirmed diagnosis of FL or DLBCL who have received at least 2 prior lines of therapy for lymphoma with evidence of disease progression and meet inclusion criteria **RESULTS/ANTICIPATED RESULTS:** Primary Endpoints: 1. Incidence and severity of adverse events as per CTCAEv5 2. Dose-limiting toxicity (DLT) of T+V, and to establish the maximum tolerated dose (MTD) of V plus fixed dose T Secondary Endpoints: 1. Incidence and Severity of toxicity and quality of life as per PRO-CTCAE and FACT-Lym 2. Overall response rate (ORR), complete response (CR) rate, partial response (PR) rate, as per Lugano criteria 3. Duration of response (DOR), progression-free survival (PFS), overall survival (OS) Exploratory Endpoints: 1. Characterization of tumor cells pre-treatment (including EZH2 mutations and BCL2 translocations) 2. Phenotypic analysis (including BCL2 expression) and quantification of the tumor microenvironment in pre-treatment samples (using image mass cytometry) Exploratory **DISCUSSION/SIGNIFICANCE:** There is a need for novel therapeutic approaches to improve the prognosis for patients with R/R NHL. Preclinical data suggests synergism between the pair. 5 Importantly, this represents a chemotherapy-free, oral regimen. If well tolerated, this could present an alternative therapeutic option for patients ineligible for more intensive therapies.

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### Influence of a Gastrointestinal Infection on Lung Immunity\*

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**OBJECTIVES/GOALS:** We aim to characterize how *Heligmosomoides polygyrus bakeri* (H. poly) alleviates murine allergic asthma which shares many characteristics of human asthma. This approach of has already identified helminth-produced human immune cell ligand “mimics” that hold great potential for next-generation clinical biologics **METHODS/STUDY POPULATION:** We examined the lung tissue of C57BL/6 mice infected with H. poly for changes in the pulmonary microenvironment. At ten days post infection, four infected mice and two co-housed uninfected mice were sacrificed, and their lung tissue harvested for examination of RNA via RT-qPCR. This design allows for the comparison between

the lung microenvironments of infected and naïve mice. In future experiments, we intend to characterize what small molecules produced by the helminth drive changes in the lung using germ-free models of H. poly infection. **RESULTS/ANTICIPATED RESULTS:** We found key differences in lung chemokines between mice infected with H. poly and naïve mice. Using a student t-test with naïve correction for variance, we were able to show significant differences in the expression of E cadherin ( $p = 0.0355$ ), CXCL10 ( $p = 0.0025$ ), CX3CL1 ( $p = 0.0029$ ), CCR2 ( $p = 0.017$ ), and IDO1 (0.0078). We also found that differences in the expression of CCL5 bordered on significant with a p-value of 0.066. The expression of most of these markers (CXCL10, CCR2, CCL5, and IDO1) was elevated in the lungs of infected mice compared to naïve controls. In contrast, E cadherin and CX3CL1 showed the opposite trend with naïve mice showing greater expression. These clear differences in lung tissue gene expression underscore the connection between the gastrointestinal and pulmonary mucosal immune compartments. **DISCUSSION/SIGNIFICANCE:** The changes are unexpected for an infection that has been shown to attenuate allergic inflammation in the lung with increases in the IFN- $\gamma$  responsive genes IDO1 and CXCL10 and inflammatory lung markers, CCL5 and CCR2. In contrast, there were decreases in inflammatory lung marker CX3CL1 and the tight junction protein E cadherin in infected mice.

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### Changes in Lipid Profiles with Progression of Pregnancy in Black Women

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**OBJECTIVES/GOALS:** Pregnant African American (Black women) have higher rates of adverse pregnancy outcomes compared to other races and routine monitoring of lipid levels is not currently in practice in prenatal care. We hypothesized that lipid profiles would show variation across pregnancy indicative of specific requirements during gestation and fetal development. **METHODS/STUDY POPULATION:** We used an untargeted lipidome analysis approach to investigate lipid metabolism with the progression of pregnancy. Pregnant Black women were recruited at prenatal clinics in Midwest (Metro Detroit, Michigan and Columbus, Ohio), women under 18 or above 45 years of age were not enrolled due to metabolic changes associated with these age groups. Women signed the consent forms and plasma samples were collected at 8-18 weeks at (T1), 22-29 weeks (T2) and 30-36 weeks (T3) of pregnancy. Samples from sixty-three women (mean age  $27.41 \pm 5.61$  years) who had term birth (completed 37 weeks of pregnancy) were subjected to “shotgun” Orbitrap high resolution/ accurate mass spectrometry. Mixed-effects models were used to quantify systematic changes in relative lipid abundances over time using R lme4 and ggplot2 packages. **RESULTS/ANTICIPATED RESULTS:** Total lipids and some major lipid classes showed a significant increase with the progression of pregnancy. Phospholipids and glycerolipids exhibited a gradual increase throughout pregnancy, while sphingolipids and total sterol lipids displayed a more pronounced increase at the T3 timepoint. Acylcarnitines, hydroxy acylcarnitines and Lyso phospholipids levels significantly decrease from T1 to T3. One of the interesting finding was that non-esterified fatty acids decreased from T1 to T2 and

increased again from T2 to T3, suggesting a possible role for these lipids during the later stages of pregnancy. The fatty acids showing this trend included key fatty acids- Linoleic Acid, Arachidonic Acid, Alpha-linolenic acid, Eicosapentaenoic acid, Docosapentaenoic acid, Docosahexaenoic acid. DISCUSSION/SIGNIFICANCE: Mapping lipid trends during pregnancy could lend support to a precision health approach to reduce perinatal health disparities among pregnant Black women. The findings from this study will be used to identify biomarkers and study associations with social and environmental factors responsible for adverse perinatal outcome in pregnant Black women.

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### Depression Moderates Independent Effects of Daily Natural Light Exposure and Activity on Daily Mood

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**OBJECTIVES/GOALS:** Ambulatory methods are useful tools to study physical and mental health in everyday life. While many studies show daily activity improves mood, the effects of daily light exposure on mood remain unknown. This study evaluated the effects of daily natural light exposure and activity on daily mood and evaluate whether depression moderate effects. **METHODS/STUDY POPULATION:** 82 adults with lifetime major depression disorder (25 current) and 49 healthy controls were recruited from the greater Chicago community (N = 131, 62% female, age M = 30.15, SD = 9.94). At baseline, participants completed the Inventory of Depression and Anxiety Symptoms to measure depression symptoms of anhedonia, or loss of pleasure. Positive and negative affect were then measured 3x daily for 14-days via self-report using smartphones while light exposure and activity were continuously recorded from a wrist-worn actigraphy device. Following prior studies, daily natural light exposure was measured as the total number of white light samples greater than 1000 lux each day. Multilevel models were used to separate within-person (daily level) from between-person (subject level) effects. **RESULTS/ANTICIPATED RESULTS:** Results revealed daily within-person activity ( $p < .001$ ) and natural light exposure duration ( $p = .035$ ) were independently associated with increased positive affect. Effects were significantly moderated by baseline anhedonia symptoms (3-way interaction:  $p = .004$ ). Natural light exposure duration only increased positive affect on lower activity days for high anhedonia and higher activity days for low anhedonia ( $ps < .018$ ). Significant results remained controlling for between-person light and activity, time of year, age, sex, negative affect, and baseline general depression symptoms. Compared to one's own daily averages, daily activity and natural light exposure may be independent pathways to boost positive affect, especially for individuals with high anhedonia symptoms. **DISCUSSION/SIGNIFICANCE:** Results suggest daily natural light exposure may be an accessible, low-cost alternative to independently increase positive affect in depression on days when activity is low. Translational applications are discussed focusing on transdiagnostic implications for physical and mental health conditions that disrupt mood and limit activity.

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### Creating Pragmatic Tools for Reliable Kidney Function Measurement in Patients with Kidney Impairment

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**OBJECTIVES/GOALS:** Estimating kidney function for drug dosing poses safety and efficacy concerns with critical medications. This study aims to develop a pragmatic method for measuring kidney function, ensuring that critical clinical decision points based on kidney function are universally applicable to all patients, leading to improved health outcomes. **METHODS/STUDY POPULATION:** This is a single-dose pharmacokinetic (PK) study to evaluate the concordance between iopamidol- and iothexol-measured glomerular filtration rate (mGFR), as determined by their respective serum clearances, in a cohort of 24 adults with varying kidney function. Participants with estimated glomerular filtration rates (CKD-EPI eGFRcr) ranging from  $>30$  to  $120$  mL/min will be recruited from the Michigan Medicine health system. Enrolled participants will be stratified into 3 kidney function groups based on conventional kidney dosing considerations. IV micro doses of iothexol and iopamidol will be administered, followed by blood sampling. PK analysis will be used to compare the clearance of these substances. The agreement between iothexol and iopamidol in measuring GFR will be assessed via bioequivalence analysis. **RESULTS/ANTICIPATED RESULTS:** We expect no statistically significant difference between iopamidol and iothexol CL due to the high similarity of iopamidol and iothexol molecular and PK properties. We also expect that the ordinary least square regression analysis of iopamidol mGFR and iothexol mGFR will show limited variability across GFR measurements. These expected results will support the use of iopamidol as a marker of mGFR and its interchangeability with the gold standard iothexol. **DISCUSSION/SIGNIFICANCE:** Addressing eGFR errors is crucial for accurately dosing critical medications. This study aims to develop a novel mGFR methodology that accommodates various kidney function levels. This will enable precision dosing and streamline clinical trials. It also eliminates biological variability, enhancing generalizability and health outcomes.

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### Development of Machine Learning Algorithms to Predict Symptomatic VTE at Time of Admission and Time of Discharge after Severe Traumatic Injury

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**OBJECTIVES/GOALS:** Clinical indicators predictive of venous thromboembolism (VTE) in trauma patients at multiple time points are not well outlined, particularly at time of discharge. We aimed to describe and predict inpatient and post-discharge risk factors of VTE after trauma using a multi-variate regression model and best of class machine learning (ML) models. **METHODS/STUDY POPULATION:** In a prospective, case-cohort study, all trauma