progression. DISCUSSION/SIGNIFICANCE: This project will determine the efficacy of FOXA2 as a biomarker in advanced prostatecancer samples, which will translate as a potentially useful tool for clinicians to use for treatment of advanced prostate cancer patients.

Regulatory Science

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Examination of Labeling for Geriatric Sub-Populations in Recently Approved Type 2 Diabetes Drugs

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OBJECTIVES/GOALS: To assess labels of drugs approved for Type 2 Diabetes (T2D) for the inclusion of geriatric sub-population data (ages 65-74, 75-84, ≥85) since January 1, 2013, in accordance with international guidance and US regulations in recognition of an aging populations and global demographics. METHODS/STUDY POPULATION: Utilizing FDA Guidance for Industry: Labeling for Human Prescription and Biological Products - Implementing the Physician's Labeling Rule (PLR) Content and Format Requirements and the International Council for Harmonization of Technical Requirements (ICH) E7 guidance "Studies in Support of Special Populations: Geriatrics" as reference for assessing labels. The Center for Drug Evaluation and Research (CDER) new drugs/biologic approvals database was filtered for drugs approved between Jan. 1, 2013 and Dec. 31, 2022 with approved T2D indications. Examined original drug labels and supplements from Drugs@FDA for geriatric use efficacy and safety wording in Section 8.5 (Use in Specific Populations, Geriatric Use), for labels. Subpopulation data in labeling for ages 65-74, 75-84, and ≥85 was analyzed. RESULTS/ANTICIPATED RESULTS: Seven T2D drugs (Trulicity, Tresiba, Adlyxin, Ozempic, Steglatro, Kerendia, Mounjaro) approved within the specified time period were analyzed. In the current examination, all labels contain information regarding efficacy differences between ages 65+ and 75+, however, none contain information on efficacy for ≥85 populations. Four of the seven drugs have been updated with increased data from further efficacy trials for older adults conducted after initial approval. The remaining three drugs have only been reworded, or not changed at all, with no further efficacy trials conducted. DISCUSSION/SIGNIFICANCE: This research shows the gap in representation of older adults in clinical trial data and T2D drugs' labeling. Despite having a higher usage of T2D drugs compared to the general population, older adults and especially the oldest-old (≥85) are underrepresented. Additional demographic requirements ensuring diversity in clinical trials is needed.

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Dihydroxyacetone, a combustion of electronic cigarettes, promotes cardiac-specific injury through metabolic and mitochondrial imbalances*

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OBJECTIVES/GOALS: Electronic cigarettes have become increasingly popular, with various combustion products generated in the process. Dihydroxyacetone (DHA), a carbohydrate made during the heating process. Exposures may reach high micromolar to low millimolar doses of DHA per day and no studies have been done to understand the effects of DHA in the heart. METHODS/STUDY POPULATION: Here, we examine if DHA contributes to these using rat cardiomyocytes, H9c2 cells, and rat cardiac tissues to DHA evaluating metabolic and mitochondrial effects. Using the cells, we will investigate metabolic and mitochondrial pathways using Seahorse, protein expression changes in nutrient sensing pathways, and understand dose-dependent effects of DHA in the heart. Metabolite pools will also be evaluated to understand the changes promoted by DHA. Oxidative stress as previously observed in other cell models will also be measured. Key findings in the cardiac cells will be investigated in the cardiac tissues exposed to DHA. RESULTS/ANTICIPATED RESULTS: We have previously shown DHA induces oxidative stress, metabolic changes, and mitochondrial dysfunction in various cell line models. Interestingly, these effects are highly cell-type dependent. E-cigarettes are known to have toxic cardiac effects, including arterial stiffness, endothelial dysfunction, vascular injury, and oxidative stress. Changes in glycolytic, fatty acid synthesis, and the citric acid cycle enzymes and metabolites were found in the H9c2 cells. We also observed increased mitochondrial ROS and fuel changes due to DHA exposure. In DHA exposed cardiac tissues, we observed oxidative stress and mitochondrial fission and fusion dynamics altered. DISCUSSION/SIGNIFICANCE: These data suggest further study at physiologically relevant doses is warranted to understand how DHA inhaled impacts the long-term health of vapers. As well as the regulation of DHA in e-cigarettes as it has been deemed as safe for topical applications and warned against inhalation.

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Use of Expanded Access at Michigan Medicine and Associations with Neighborhood Factors

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OBJECTIVES/GOALS: Socioeconomic status (SES) affects risk of disease and access to therapies. The expanded access (EA) pathway allows for the clinical use of investigational products for patients who have serious illness but no Food and Drug Administration (FDA)-approved therapeutic options. The SES of patients who receive EA is unknown. METHODS/STUDY POPULATION: We reviewed the patients who were approved for treatment through a single-patient EA pathway between 2018 and 2023. Using Michigan Medicine (MM) DataDirect software linked to the MM electronic medical record system, we linked the EA pathway patients to neighborhood data from the National Neighborhood Data Archive (NaNDA) to compare neighborhood related markers of affluence among EA patients and others treated at MM. We used descriptive statistics to compare variables between EA pathway patients and

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residents of the state of Michigan or the local county surrounding MM (Washtenaw County), using US Census tract data to provide context for these findings. RESULTS/ANTICIPATED RESULTS: MM patients who received EA treatments were more likely to come from neighborhoods that showed markers of high SES compared to residents of the state of Michigan but not Washtenaw County. This includes the proportion of persons living in poverty (12.5% EA / 13.4% Michigan / 12.4% Washtenaw) and education in the form of a bachelor's degree or higher (32.2% / 30.6% / 57.2%). This varied by the disease being treated. Oncology patients were more likely to be from areas with less poverty and more education (12.4% / 76.8%) than the EA average. EA patients being treated for infectious diseases were from areas with more poverty and less education (13.5% / 26.7%). DISCUSSION/SIGNIFICANCE: Patients treated at Michigan Medicine using treatments obtained through the EA pathway came from areas that were, on average, more affluent than residents of the state of Michigan as a whole. This finding warrants more research to ensure equitable access to these therapies for patients in disadvantaged neighborhoods.

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Examining Participant Representation in Atopic Dermatitis Clinical Trials from 2011-2022

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OBJECTIVES/GOALS: This study seeks to comprehensively evaluate the extent to which participants in clinical trials (CT) for Atopic Dermatitis (AD) accurately mirror the demographics and characteristics of the broader AD-affected populations. We will achieve this objective by analyzing data from AD CTs spanning the years 2011 to 2022. METHODS/STUDY POPULATION: We examined completed trials for 10 FDA approved treatments for AD, utilizing data sourced fromclinicaltrials.gov [http://clinicaltrials.gov]. In light of the increased number of AD clinical trials over the past decade, we tailored our search parameters to encompass all trials related to approved treatments from 2011-2022. To assess the characteristics of the participant population in these trials, information including inclusion and exclusion criteria, age, location, sex, and disease severity were collected for each trial. Furthermore, race and ethnicity data were also extracted and analyzed. Additionally, comparisons were drawn between trials completed before and after April 2017, when the FDA began requiring that researchers publish race and ethnicity data toclinicaltrials.gov [http://clinicaltrials.gov]. RESULTS/ANTICIPATED RESULTS: Across 67 CTs examined, 45% of trials were restricted to adult patients, 28% were restricted to pediatric patients, and 27% included both. 77% of CTs occurred in urban settings and 23% occurred in rural settings according to the The Economic Research Service definition. 36% of CTs included mild-to-moderate AD patients, and 64% of CTs included moderate-to-severe AD patients. Race distribution of CTs revealed 67% White, 14% Black/African American, 16% Asian, and 3% others. 13% of participants identified as Hispanic or Latino. With further analysis, we will determine whether there is a difference in ethnic distribution between trials completed before and after April 2017, when the FDA started requiring race/ethnicity data to be submitted. DISCUSSION/SIGNIFICANCE: The findings highlight a significant concern in AD CTs: the insufficient representation of Black and Asian populations. The findings emphasize the need for a more inclusive selection process that accurately reflects the diversity of patients. Failing to do so could undermine the assessment of treatment effectiveness in such populations.

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A Comparison of Regulatory Mechanisms for the Approval of Herbal Medicines

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OBJECTIVES/GOALS: To compare the herbal medicine (HM) programs of the U.S. to those of different countries–including the European Union, South Korea, China, and India–and to examine each regulatory body's process for obtaining market approval for HM drugs. METHODS/STUDY POPULATION: The European Union, South Korea, China, and India's respective HM regulatory programs were examined and compared to the U.S. FDA's HM process. These specific regulatory bodies were chosen based on the country's long history with HM and/or the robustness of their existing HM review processes. International HM programs were researched using official government websites and journals published by independent, external research institutions that were accessed via USC's library services. Data regarding the efficacy of HM policies such as HM IND approval rates, number of marketed HM drugs, and establishment of unique HM sectors will be collected. RESULTS/ANTICIPATED RESULTS: Investigational New Drug (INDs) applications regarding HM from each country will be categorized and displayed according to their approval status in order to provide insight on a HM program's efficiency. Results also included a table displaying common challenges for approval for HM drugs across federal regulatory bodies. If applicable, effective solutions implemented to address some of these obstacles that proved to be effective will also be displayed in the form of a table. DISCUSSION/SIGNIFICANCE: Tables displaying the collective flaws of international HM programs and the resulting regulatory solutions can provide clearer guidance for companies seeking to submit HM INDs and for the U.S. FDA seeking to develop improved HM regulations.

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A Multi-Institutional Look at Single-Patient Expanded Access Submissions

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OBJECTIVES/GOALS: Physicians can request the clinical use of investigational products for their patients through an FDA pathway called Expanded Access (EA). Most evaluations of EA focus on the FDA submission only. We sought to evaluate these requests through

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