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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