development. OBJECTIVES/GOALS: Spray-dried dispersion (SDD) tablet formulation is an approach to increase oral drug solubility and absorption. Methods to predict SDD performance in humans are poorly developed. We aim to develop an in vivo in vitro correlation (IVIVC) between in vitro dissolution and in vivo absorption of itraconazole SDD tablets. METHODS/STUDY POPULATION: This research project involves tablet manufacturing, in vitro dissolution experiments, and a clinical study. We manufactured fast-, medium-, and slow-release SDD tablets containing amorphous solid dispersion of itraconazole (100 mg) and different grades of the polymer hypromellose acetate succinate (HPMC-AS). Tablets differed in slug pressure, tablet compression force, and formulation composition. Dissolution studies were performed using the United States Pharmacopeia (USP) type II apparatus. The clinical study is an ongoing randomized, cross-over, open-label, fasted, single-dose trial in healthy participants (n=12). An IVIVC will be created by comparing the rank order of drug in vitro dissolution with in vivo absorption. RESULTS/ANTICIPATED RESULTS: Tablet manufacturing was successful, and the tablets displayed the same dissolution rate ranking order as anticipated. Fast-release tablets showed the highest percentage of drug dissolved by 10 min (74%) compared to medium- (62%) and slow-release (1.2%) tablets. Percentage drug dissolved differs by at least 10% at all time points among the different release-rate tablets. The clinical study is currently ongoing, and we expect that the pharmacokinetic (PK) profiles differ among the different tablets. We predict that the rank order of tablet absorption in humans will agree with the order of drug dissolved observed in the dissolution experiments. DISCUSSION/SIGNIFICANCE OF FINDINGS: Spray-dried dispersions are a formulation method to try to improve drug solubility and oral drug absorption. This research will elucidate manufacturing parameters that can impact tablet performance and expand on the ability of in vitro dissolution to predict human PK and streamline drug development of poorly soluble drug candidates.

Translational Science, Policy, & Health Outcomes Science

ABSTRACT IMPACT: Knowledge of which aspects of social connectedness most strongly associate with caregiver health and health behaviors can inform intervention targets to improve caregiver health

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Daily relationship between social connectedness and health behaviors among dementia family caregivers

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ABSTRACT IMPACT: Knowledge of which aspects of social connectedness most strongly associate with caregiver health and health behaviors can inform intervention targets to improve caregiver health

OBJECTIVES/GOALS: Stressed dementia caregivers are at risk of poor health. Social connectedness may reduce adverse health effects, yet it is unknown about which aspects relate most strongly to health. This is a barrier to intervention development. Our study identifies aspects of social connectedness most strongly associate with caregivers’ daily health behaviors. METHODS/STUDY POPULATION: Data. Enrolled spousal caregivers completed 14 consecutive days of online surveys. Measures. We examined multiple health behaviors each day, which included: 1) number of occurrences of 3 potential binge-eating behaviors (range 0 to 30), 2) whether participants engaged in at least 30 minutes of physical activity, and 3) perceived sleep quality, rated 1 (very bad) to 5 (very good). We also examined a count of health symptoms caregivers experienced (e.g., backache; range: 0 to 7). Measures of social connectedness included: spousal emotional support, perceived spousal appreciation, emotional support from any source, and loneliness. Analysis. We applied bivariate multi-level mixed effects models to examine the association between each aspect of social connectedness and health behaviors day-to-day. RESULTS/ANTICIPATED RESULTS: Since November 2020, 5 of N=40 participants were enrolled, of whom 3 had completed all diary surveys. Participants were women ages 59 to 73, and included 4 non-Hispanic white and 1 Hispanic caregivers. Data included 51 days of surveys (93% adherence). No
Black patients with triple negative breast cancer (TNBC).

ABSTRACT IMPACT: Reversing tumor microenvironment (TME) immunosuppression will help to increase the overall efficacy of treatment of chemo-resistant triple negative breast cancer (TNBC) and mitigate racial disparities in treatment response. OBJECTIVES/GOALS: We have developed an ex-vivo whole tissue culture model to test the feasibility of reversing local immunosuppression in TME by chemokine modulatory (CKM) regimen. Our current objective is to analyze the molecular changes in CKM-treated chemoresistant TNBC from White and Black women and identity factors determining response to CKM. METHODS/STUDY POPULATION: Freshly resected residual TNBC from 20 White and 20 Black women ≥18 yrs old treated with neoadjuvant chemotherapy (NAC) will be procured. Tumor explants will be prepared & cultured in the absence and presence of CKM (Interferon-β, TLR3 agonist rintatolimod and COX-2 inhibitor celecoxib). Chemokines implicated in cytotoxic T-lymphocyte (CTL)- & MDCS/ Treg attraction will be analyzed using Taqman & ELISA. We will have 80% power to detect a 0.7 standard deviation difference in chemokines between untreated & treated samples within and between cohorts using ANCOVA. Bulk RNA sequencing will be performed on both untreated & treated samples from CKM responding (highest aggregate increase in CTL- and highest decrease in Treg/MDCS-favoring chemokines in the top quartile) and non-responding (bottom quartile) tissues. RESULTS/ANTICIPATED RESULTS: Our preliminary data show that Black patients (pts) with breast cancer (BC) have an immunosuppressive TME associated with poor outcomes. This is similar to other existing TME associated with poor outcomes. This is similar to other existing TME associated with poor outcomes.

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