vaccination strategy may have a clinical benefit in reducing influenza infections in plasma cell disorder patients and thus may have practice changing implications. Final analyses of serologic responses, clinical correlates of response, and cell-mediated immune correlates may provide valuable insights into in vivo "immune-competence" in patients with plasma cell disorders.

**2198**

## Gender differences in the pharmacology of buprenorphine sublingual tablets in Hispanics/Latinos: An underrepresented population

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OBJECTIVES/SPECIFIC AIMS: The objective of this study is the pharmacology of sublingual Buprenorphine in Hispanics/Latino men and women. Specifically we plan to: (1) Administer sublingual buprenorphine to Hispanic/Latino men and women volunteers, and measure the circulating amounts of the drug in the bloodstream as a function of time; that is, pharmacokinetics of buprenorphine. The goal of the proposed study is to evidence that there are gender and ethnic differences in the pharmacokinetics of sublingual buprenorphine between not only Hispanics/Latinos and non-Hispanics/Latinos (Caucasian), but also within Hispanic/Latino men and women. METHODS/STUDY POPULATION: We are proposing a phase 1 of buprenorphine using 12 healthy volunteers. To test for differences in pharmacokinetics between Hispanic/Latino men and women, 6 Hispanic/Latino men, and 6 Hispanic/Latino women 21 years of age and older will be recruited. The volunteers should be living in Puerto Rico, and must have both parents born in Puerto Rico. Sublingual buprenorphine will be administered using a low dose of 16 mg one time only. Blood samples will be collected from each volunteer at $t = 0$, 1, 2, 4, 6, 8, 12, and 24 hours after administration. The amount of circulating drug in the bloodstream of the volunteers will be measured using liquid chromatography combined with mass spectrometry. Pharmacokinetic obtained parameters will be maximal plasma concentration, minimal plasma concentration, predose concentration, 24 hour post predose concentration, the time for maximum concentration. The area under the curve will be determined by the trapezoidal rule. Male Versus female data will be compared using 2-tailed *t*-test. RESULTS/ANTICIPATED RESULTS: We anticipate that: (1) Hispanic/Latino women will have longer circulating times of the drug in the bloodstream and higher maximum concentrations, compared with men. (2) Hispanic/Latino men and women will have higher amounts of the circulating drug, compared with already reported pharmacokinetic data of non-Hispanic Caucasian men. DISCUSSION/SIGNIFICANCE OF IMPACT: Gender differences have been elucidated in the prevalence rates of substance abuse, health service utilization, treatment outcomes, and physiological consequences of drug consumption in the United States. It is known that in general, women progress from drug use to dependence must faster than men; women also suffer more severe physical and emotional consequences than men, yet women seek treatment for drug addiction in lower rates compared with men. Women also show lower pharmacological treatment effectiveness as they are less likely to feel satisfied upon entering a substance abuse treatment and they show higher cravings. Sublingual buprenorphine is a very popular and relatively new medication used primarily for opiate addiction since 2002. Gender differences have been elucidated in the pharmacology of buprenorphine sublingual tablets used for the treatment of opioid addiction. One study showed that women had higher concentrations of circulating parent drug and it is metabolites compared with men. One metabolite in particular norbuprenorphine was found in almost double the plasma concentration in women. Interestingly, gender differences were not pursued at all by the Pharmaceutical Company sponsoring the approval of the sublingual Buprenorphine by the FDA. The cytochrome enzyme CYP 3A4 responsible for the metabolism of Buprenorphine has higher activity in Caucasian/African American women compared with men. However these studies failed to design and recruit significant amount of patients with Hispanic ethnicity to adequately elucidate the gender differences within this ethnic group. Higher plasma concentrations and longer circulation times of a drug may result not only in lower efficacy outcomes but also higher toxicity and undesired effects. Unfortunately, the lack of pharmacological effectiveness and lack of satisfaction in women undergoing drug treatment programs has not been adequately studied to understand the gender difference in pharmacological treatment outcomes between Hispanic/Latino men and women. Due to the under-representation of Hispanic/Latino men but most importantly women in s studying the pharmacology of sublingual Buprenorphine, and considering the well-established gender difference of the principal enzyme (CYP 3A4) responsible for the pharmacology of Buprenorphine, we are proposing a pilot study of the pharmacology of sublingual Buprenorphine in Hispanic/Latino volunteers living in Puerto Rico with equal number of male and female patients. We expect our research to clinically and scientifically elucidate the gender differences of sublingual buprenorphine for opioid addiction in Hispanics/Latinos. The outcome of such research will be the foundation of subsequent clinical studies that aim in updating the current standard of care for Hispanic/Latino men and women that require therapy for opioid addiction.

**2203**

## Engraftment and gene expression of an HIV resistant immune system in a Phase I trial of an HIV stem cell gene therapy strategy

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OBJECTIVES/SPECIFIC AIMS: To date, only 1 documented case of an individual cured of HIV has been reported. He received an allogeneic bone marrow transplant with cells harboring an HIV-resistant genotype. To mimic this result, we have initiated a Phase I to evaluate the safety of an autologous stem cell gene therapy bone marrow transplant in HIV-related lymphoma patients. METHODS/STUDY POPULATION: The first cohort of patients will receive a 1:1 ratio of unmanipulated CD34 hematopoietic stem cells (HSC) and lentivector modified CD34 HSC expressing a combination of HIV-resistant genes and a selectable marker for cell sorting prior to transplantation. Safety of the HIV-resistant stem cells will be assessed by evaluating engraftment, expression of the anti-HIV genes, and the stability and sequence of the vector. RESULTS/ANTICIPATED RESULTS: One patient has been enrolled and transplanted with the HIV-resistant stem cells. After 1 and 2 months post-transplant, patient blood samples were received, processed for genomic DNA, analyzed by quantitative PCR (qPCR), and displayed successful engraftment of 16 and 12 vector copies per 100 cells, respectively. Expression of all anti-HIV genes was confirmed by qPCR. PCR on genomic DNA confirmed the correct sizes and sequences of the integrated vector and confirmed the successful engraftment of our gene modified cells. Currently, we are enrolling more patients into the trial. DISCUSSION/SIGNIFICANCE OF IMPACT: If successful, this therapy has the potential to change HIV treatment.

**2207**

## A Phase I dose escalation trial of nab-paclitaxel and fixed dose radiation in patients with unresectable or borderline resectable pancreatic cancer

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OBJECTIVES/SPECIFIC AIMS: Patients with locally advanced pancreatic cancer typically have poor outcomes, with a median survival of ~16 months. Novel methods to improve local control are needed. Nab-paclitaxel (abraxane) has shown efficacy in pancreatic cancer and is FDA approved for metastatic disease in combination with gemcitabine. Nab-paclitaxel is also a promising radiosensitizer based on laboratory studies, but it has never been clinically tested with definitive radiotherapy for locally advanced disease. METHODS/STUDY POPULATION: We performed a phase 1 study using a 3 + 3 dose-escalation strategy to determine the safety and tolerability of dose escalated nab-paclitaxel with fractionated radiotherapy for patients with unresectable or borderline resectable pancreatic cancer. Following induction chemotherapy with 2 cycles of nab-paclitaxel and gemcitabine, patients were treated with weekly nab-paclitaxel and daily radiotherapy to a dose of 52.5 Gy in 25 fractions. Final dose-limiting toxicity (DLT) determination was performed at day 65 after the start of radiotherapy. RESULTS/ANTICIPATED RESULTS: Nine patients received nab-paclitaxel at a dose level of either 100 mg/m$^2$ ($n = 3$) or 125 mg/m$^2$ ($n = 6$). One DLT (grade 3 neuropathy) was observed in a patient who received 125 mg/m$^2$ of nab-paclitaxel. Other grade 3 toxicities included fatigue (11%), anemia (11%), and neutropenia (11%). No grade 4 toxicities were observed. With a median follow-up of 8 months (range 5–28 months), median survival was 19 months and median progression-free survival was 10 months. Following chemoradiation, 3 patients underwent surgical resection, all with negative margins and limited tumor viability. Of the 3 patients, 2 initially had borderline resectable tumors and 1 had an unresectable tumor. Tumor (SMAD-4, Caveolin-1) and peripheral (circulating tumor cells and microvesicles) biomarkers were collected and are being analyzed. DISCUSSION/SIGNIFICANCE OF IMPACT: The combination

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