**eMERGE Network Proposal for Analysis**

Project/Manuscript Concept Sheet

|  |  |
| --- | --- |
| **Submission Date** | January 18, 2017 |
| **Reference Number** | NT206 |
| **Project Title** | Outcomes in Asthma Patients Treated in Accordance with NHLBI Guidelines |
| **Tentative Lead Investigator (first author)** | Nikita Sood |
| **Tentative Senior Author (last author)** | H Hakonarson |
| **All other authors**  | Erik Hysinger, Patrick Sleiman, Frank Mentch, Lyam Vazquez, John Connolly, Berta Almoguera, members of the Outcomes WG and other interested members of eMERGE  |
| **Sites Involved** | All interested sites |
| **Background / Significance** | Beta2-agonist medications, such as albuterol and salmeterol, are commonly used to treat asthma, but are not effective in all patients. Poor response may present as decreased lung function and increase in pulmonary exacerbations. Several single nucleotide polymorphism (SNPs) have been correlated with drug-responsiveness, including rs1042713 and rs1042714 (both *ADRB2*), rs730012 (*LTC4S*), and rs37972 *GLCCI1*). We propose to study asthma outcome, as evidenced by exacerbation frequency, in patients requiring beta2-agonist and other asthma medications. Patients will be stratified by genotype, severity and adherence to NHLBI asthma treatment guidelines. Preliminary data from CHOP, presented to the Outcomes WG in November 2016, found that exacerbation frequency was significantly different between subjects who adhered to asthma therapy guidelines vs. not, and that two SNPs (rs1042713 and rs1042714) showed association with reduced response in subjects who adhered to guidelines (2 copies of respective risk alleles had most exacerbations. Ultimately, an exploration of pharmacogenetic relationships underling asthma response may lead to improved treatment guidelines.  |
| **Outline of Project** | This project plans to investigate the inconsistent outcomes and varying approaches to care in asthma patients, as well as the potential for a genetic component in determining patient outcomes regardless of guideline adherence. The study had two main aims: (1) to investigate whether stricter adherence to the 2007 NHLBI guidelines was correlated with better patient outcomes and (2) to investigate whether cases with good guideline adherence but worse outcomes could be explained by genetic factors. |
| **Desired****Variables (essential for analysis****indicated by \*)** | eMERGE 1,2,3 genotypes and phenotype data based on the CHOP asthma algorithm, updated with ICD-10 codes: Cases of asthma are defined as age greater than 4 years, a primary ICD code for asthma on at least two separate calendar days, as well as documented prescriptions for asthma-related medication.  |
| **Desired data** | Outcomes data: (1) results of asthma control tests, (2) results of spirometry tests, (3) asthma-related ER visit frequency, (4) asthma-related ICU visit frequency, (5) asthma-related observation visit frequency, (6) asthma-related inpatient hospitalization frequency, and (7) asthma-related exacerbation frequencyNHLBI guideline data: (1) patient provided with an asthma care plan, (2) patient given an asthma control test, (3) patient had spirometry tests, and (4) patient visited at least every 200 days.Patient compliance data: if compliance was commented on within provider notes, patients were given a compliance score based on percentage of notes that commenting good compliance (1 for 0-20% good compliance, 2 for 20-40% good compliance, 3 for 40-60% good compliance, 4 for 60-80% good compliance, and 5 for 80-100% good compliance).Data from 3 genotypedSNPs: rs1042713, rs1042714, and rs37972 |
| **Planned Statistical Analyses** | Covariates are asthma severity, sex, race, and patient compliance. |
| **Ethical considerations** | None |
| **Target Journal** | American Journal of Respiratory and Critical Care Medicine |
| **Milestones\*\*** | Re-development of phenotype algorithm, with ICD-10 codes: 2/31/17Internal validation of phenotype algorithm: 3/14/17Implementation of phenotype algorithm: 4/31/17Analyses of array data: 5/30/17Submission of manuscript: 8/31/17 |