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POSTER ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Clinical Results of a Randomized Placebo Controlled Trial of Inhaled Mometasone to Promote Reduction in Vaso-Occlusive Events (IMPROVE-II)

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Introduction:
A subset of patients living with sickle cell disease (SCD) who do not meet diagnostic criteria for asthma exhibit episodic cough or wheeze (ECW), and this is associated with higher rates of vaso-occlusive pain crisis and acute chest syndrome. ECW may be caused by pulmonary inflammation from SCD. In the former IMPROVE trial, 54 patients with SCD and ECW were randomized to receive 16 weeks of placebo or mometasone furoate, an inhaled corticosteroid used to treat pulmonary inflammation. Treatment with mometasone was associated with significant reductions in daily pain, markers of hemolysis, and soluble vascular cell adhesion molecule (sVCAM) (a biomarker of disease severity in SCD) compared to placebo. The IMPROVE-II trial evaluated whether treatment with mometasone over a longer period could improve clinical and biological endpoints in non-asthmatic patients with SCD and ECW. We report here the clinical outcomes from the IMPROVE-II trial.
Methods:
We conducted a randomized, placebo-controlled, single-center interventional trial. Patients with SCD without asthma were randomized to receive either mometasone furoate 220 mcg or placebo inhaled powder for 48 weeks followed by a 4-week wash out. Key inclusion criteria included age > 18 years with SCD genotype HbSS/HbSβ0 at stable baseline who endorsed ECW. Patients were excluded if they had >15 emergency department (ED) visits for vaso-occlusive pain crisis in the past 12 months or if other treatments for SCD (i.e. hydroxyurea, L-glutamine) were being titrated. The primary outcome was the change in soluble vascular cell adhesion molecule (sVCAM) level with treatment. Clinical outcomes included ED visits and hospitalizations for any reason, and health care visits for acute chest syndrome, pneumonia, stroke, or transient ischemic attack, as well as daily pain (self-report 1-10 scale), and 6 Minute Walk. Adaptive covariate randomization was used to balance covariates including hydroxyurea use (yes/no), age, and previous rate of ED use.
Results:
A total of 80 patients were randomized and 77 received study treatment; 40 were assigned to mometasone and 37 to placebo (Figure 1). There were no significant differences between treatment groups in patient demographics (Table 1). Treatment with mometasone was associated with higher rates of acute care visits for vaso-occlusive crisis (4 (2/19) vs 1 (1/3) /patient year (50%(25%/75%), p<0.001), hospitalization for acute chest syndrome (mean 0.2 vs 0.1/patient year, p=0.05) and ED utilization (2 (1/5) vs 2 (1/4) /patient year (50%(25%/75%), p0.01). Laboratory outcomes including sVCAM are not yet resulted.
Adverse events that were reported by more than 5% of patients are listed in Table 1; there was no difference between rates of adverse (<5%) events between mometasone and placebo. There were no deaths during the study.
Conclusions:
In individuals with SCD and ECW who do not have asthma, long-term treatment with inhaled corticosteroids did not improve clinical outcomes and may be harmful as they were associated with higher rates of acute care visits for pain crisis, ED visits, and acute chest syndrome. Further analyses of biological endpoints and clinical laboratory data are needed to fully elucidate the effects of inhaled corticosteroids in SCD.

Disclosures Cohen: *Sanofi:* Other: Member of an independent data safety monitoring board; *Forma Therapeutics:* Consultancy, Other: member of a one-time advisory board meeting about clinical trial endpoints .

OffLabel Disclosure: Mometasone to reduce vaso-occlusive events in sickle cell disease

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Figure 1: CONSORT Diagram

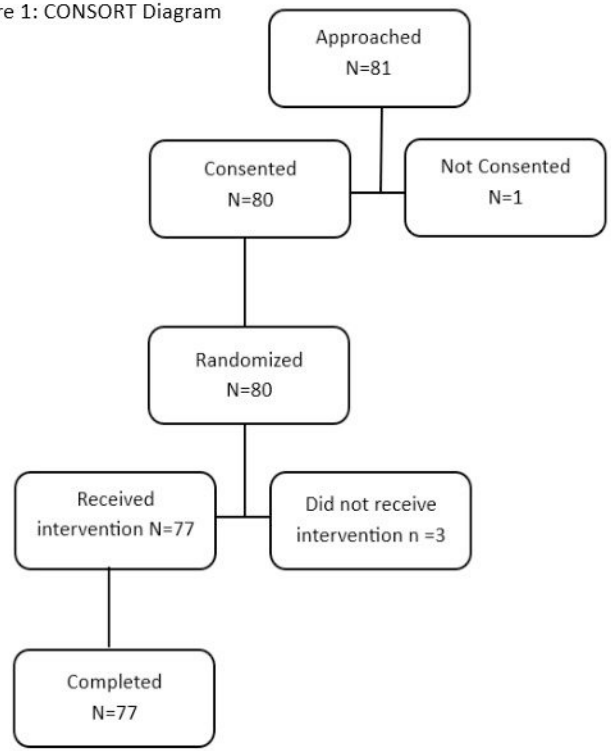

Table 1: Clinical Outcomes

	Mometasone	Control	p
N	40	37	
Patient Demographics			
Sex (%Female)	65%	48%	0.2
Race (% Black)	79%	73%	0.7
Genotype (%HbSS/HbSβ)	1.00	1.00	1
Age (mean ± SD)	36.0±11.6	31.5±8.6	0.09
Hydroxyurea (% taking)	76%	72%	0.7
Clinical Outcomes			
Acute Visit for Pain (/patient year) (50% (25%/75%)	4 (2/19)	1 (1/3)	<0.001
Acute Chest (/patient year) (mean)	0.2	0.1	0.05
Emergency Department Visit (/patient year) (50% (25%/75%)	2 (1/5)	2 (1/4)	0.01
Hospitalization (/patient year) (50% (25%/75%)	1 (1/2)	2.5 (1/3.5)	0.7
Daily Pain Rating (mean ± SD)	2.0±2.1	1.8±2.0	0.7
6 Minute Walk Test M (mean ± SD)	369.3±57.9	384.1±65.7	0.3
Adverse Effects			
sore throat	28%	32%	0.8
hoarse voice	25%	30%	0.8
thrush	15%	5%	0.3
pneumonia	8%	5%	0.9
cough	5%	14%	0.4
all other (<5%)	24%	35%	0.4

Figure 1