Steroid insensitivity and the heterogeneous nature of asthma represent a significant clinical challenge for patients with severe asthma. The use of peripheral blood mononuclear cells (PBMC) in recent studies has allowed researchers to demonstrate that poor steroid response could be due to corticosteroid insensitivity in immune cells. These cells have been used as a model to investigate the underlying molecular mechanisms of corticosteroid resistance. These models were however inconclusive and have failed to consider asthma phenotypes. Our aim was to determine in vitro corticosteroid sensitivity of isolated PBMCs in T1/2 high and T1/2 low patients. Severe asthma patients as classified by the Global Initiative for Asthma were recruited and divided into T1/2 high and T1/2 low cohorts based on fractional exhaled nitric oxide (FeNO). Isolated PBMCs were stimulated with oCD3/28 alone or in the presence of dexamethasone (10−10 M-10−6 M). IL-5, IL-13 and IL-17 cytokine release were measured using ELISA. Correlation studies were carried out to determine whether the LogIC50 or FeNO correlated with markers of asthma severity. PBMCs stimulated with oCD3/28 showed significant IL-5 and IL-17 release in T1/2 low but not T1/2 high patients. Production of IL-5 or IL-7 was dose-dependently suppressed by dexamethasone with different potencies. IL-13 was only significantly stimulated in T1/2 low patients and did not show suppression by dexamethasone. A significant negative correlation between oCD3/28 stimulated IL-17 production and FeNO was observed. Overall, PBMCs from severe asthmatics retain cell responsiveness to TCR engagement with production of T H2 and T H17 cytokines and inhibition by dexamethasone. Additional studies comparing T1/2 high vs T1/2 low patients are required to determine whether differences in in vitro CS response exist between these 2 categories of patients.

Conclusion There is a high prevalence of asymptomatic parasitic infection within our cohort, suggesting local patients who have an eosinophilia should be screened for helminth disease even in the presence of another cause eosinophilia. Furthermore, we recommend all patients being assessed for a biologic that would inhibit Th2 responses, such as Mepoluzimab, should be screened for latent Strongyloides stercoralis infection given the danger of hyper-infection upon immunosuppression.