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**Title:** ADEPT, airway disease endotyping for personalized treatment: Interim analysis of asthma patients

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**Body:** Background ADEPT is a non-interventional study to characterize the clinical and molecular profiles of healthy, asthmatic, and COPD patients Methods Gene signatures of steroid up- and down- regulated genes were generated from in vitro stimulations of primary human airway cells from commercial sources. These steroid gene signatures were evaluated in the ADEPT asthma biopsies using GSEA to evaluate steroid responsiveness. Results The interim analysis included 15 healthy nonatopic subjects and 15, 13, and 11 mild, moderate, and severe asthmatics, respectively. The steroid down-regulated gene signature was enriched in moderate and severe but not mild asthma. The up-regulated signature was suppressed in mild asthma, and enriched in moderate but not severe asthma (Table 1). Asthma-related genes, including ALOX15, MUC5AC, and periostin, were each over-expressed in at least 2 asthma groups. Expression of B

cell, T cell, mast cell genes was decreased in moderate and severe asthma.

#### Steroid gene signature enrichment in asthma

Signature	Mild	Moderate	Severe
Steroid, Down regulation	0.30 (-0.59)	0.015 (-0.76)	<0.0001 (-0.93)
Steroid, Up regulation	0.098 (-0.53)	0.0073 (0.78)	0.74 (-0.32)

Nominal p-value (enrichment score), with healthy nonatopic control group as reference

Conclusions Differential enrichment of the steroid gene signature was detected and corresponded to severity group. Confirmation of the unique findings in the severe asthma group awaits testing with the complete dataset. The unexpected findings in severe asthma may help elucidate mechanisms underlying steroid resistance.