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Drug metabolizing enzymes and transporters may help determine effective budesonide dosing in EoE

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INTRODUCTION

- Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder and its trial-and-error approach of EoE treatment can delay effective treatment
- Budesonide is a known CYP3A5 substrate and P-gp substrate
- The objective is to determine if an EoE patient's CYP3A5 and P-gp genotype and/or expression affects the response to topical budesonide treatment
- If true, CYP3A5 genotype can be determined prior to the initiation of budesonide

METHOD

- Single center retrospective study, with ongoing patient recruitment from the established Gastroenterology Repository for Information in Pediatrics biorepository (GRIP)
- For this interim analysis, DNA and mRNA were obtained from 23 patients
- Blood samples were analyzed for *3, *6, and *7 by qPCR
- Expression for CYP3A4 and ABCB1 were measured by Bio-Rad Droplet Digital PCR (ddPCR) platform

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Sample ID	CYP3A5 Genotype	ABCB1 Ratio	CYP3A4 Ratio
13U	*3/*3		0.0007
35U	*1/*1		
74D	*1/*3		
170U	*3/*3		
172U	*3/*3	0.0128	0.0007
198U	*3/*3	0.0003	
174D	*3/*3		0.0004
174M	*3/*3		
187D	*1/*1		
187M	*1/*1	0.00	0.0000
191D	*3/*3		
191M	*3/*3		
223D	*3/*3		
223M	*3/*3		
225D	*3/*3		
225M	*3/*3		
228D	*3/*3	0.0003	
228M	*3/*3		
235D	*3/*3		0.0000
236D	*3/*3	0.0000	
252D	*3/*3		
253D	*3/*3	0.0000	
253M	*3/*3		
269D	*3/*3		
270D	*3/*3		0.0000
273D	*3/*3		
279D	*1/*6	0.0000	0.0003
283D	*3/*3		0.0003

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RESULTS

- CYP3A4/GAPDH expression ratios of this small cohort shows that mRNA expression does not vary between genotype
- CYP3A4 and ABCB1 expression are low in the esophagus
- This cohort had both wild type and variant alleles
- The number of eosinophils are significantly decreased while on budesonide (p=0.0028)
- ddPCR successfully measured CYP3A4 and ABCB1 expression in esophageal tissue samples

DISCUSSION

- Initial results support low expression of CYP3A4 even in pediatric population
- So far, no significant difference in expression is seen between the wild type allele and variant alleles.
- CYP3A5 genotype does not correlate with CYP3A4 expression
- Future studies will involve collection of more patient samples for evaluation of CYP3A5 genotype and response to treatment.
- This initial study supports the need for ongoing research in budesonide precision therapeutics