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

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INTRODUCTION

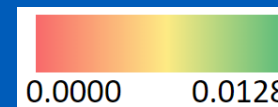
- Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder and its trial-and-error approach of EoE treatment can delay effective treatment
- Budesonide is a known CYP3A* substrate and P-gp substrate
- The objective is to determine if an EoE patient's CYP3A* and P-gp genotype and/or expression affects the response to topical budesonide treatment
- If true, CYP3A* 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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CYP3A5 Genotype	ABCB1 Ratio	CYP3A4 Ratio
*3/*3		0.0007
*1/*1		
*1/*3		
*3/*3		
*3/*3	0.0128	0.0007
*3/*3	0.0001	
*3/*3		0.0004
*3/*3		
*1/*1		
*1/*1	0.00	0.0000
*3/*3		
*3/*3		
*3/*3		
*3/*3		
*3/*3		
*3/*3		
*3/*3	0.0001	
*3/*3		
*3/*3	0.0004	0.0000
*3/*3		
*3/*3		
*3/*3		0.0000
*3/*3		
*1/*6	0.0004	0.0000
*3/*3		



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

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