

Improvement in fat-soluble vitamin levels following highly-effective CFTR modulator use in children with CF

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BACKGROUND

- People with CF are at risk for **malnutrition** and **fat-soluble vitamin deficiencies** due to pancreatic insufficiency and fat malabsorption
- Highly effective CFTR modulators, **ivacaftor** and **elexacaftor/tezacaftor/ivacaftor (ETI)**, substantially improve CFTR activity, lung function and nutritional status (weight and body-mass index) in people with CF with responsive genetic mutations
- Highly effective modulators may also **improve pancreatic function**
- Little is known regarding the effect of these medications on the **levels of fat-soluble vitamin levels** (Vit. A, D and E) following treatment with ivacaftor and ETI

METHODS

- **Retrospective study** of children with CF who had at least two annual evaluations including vitamin A, D and E serum measurements prior to **ivacaftor** or **ETI** start date and at least one evaluation ≥ 3 months post-modulator start date
- Data collected included demographics, CF diagnostic data, pancreatic status, nutritional status, and lung function
- Summary statistics were calculated and vitamin values were compared pre and post modulator within group via **Wilcoxon tests**

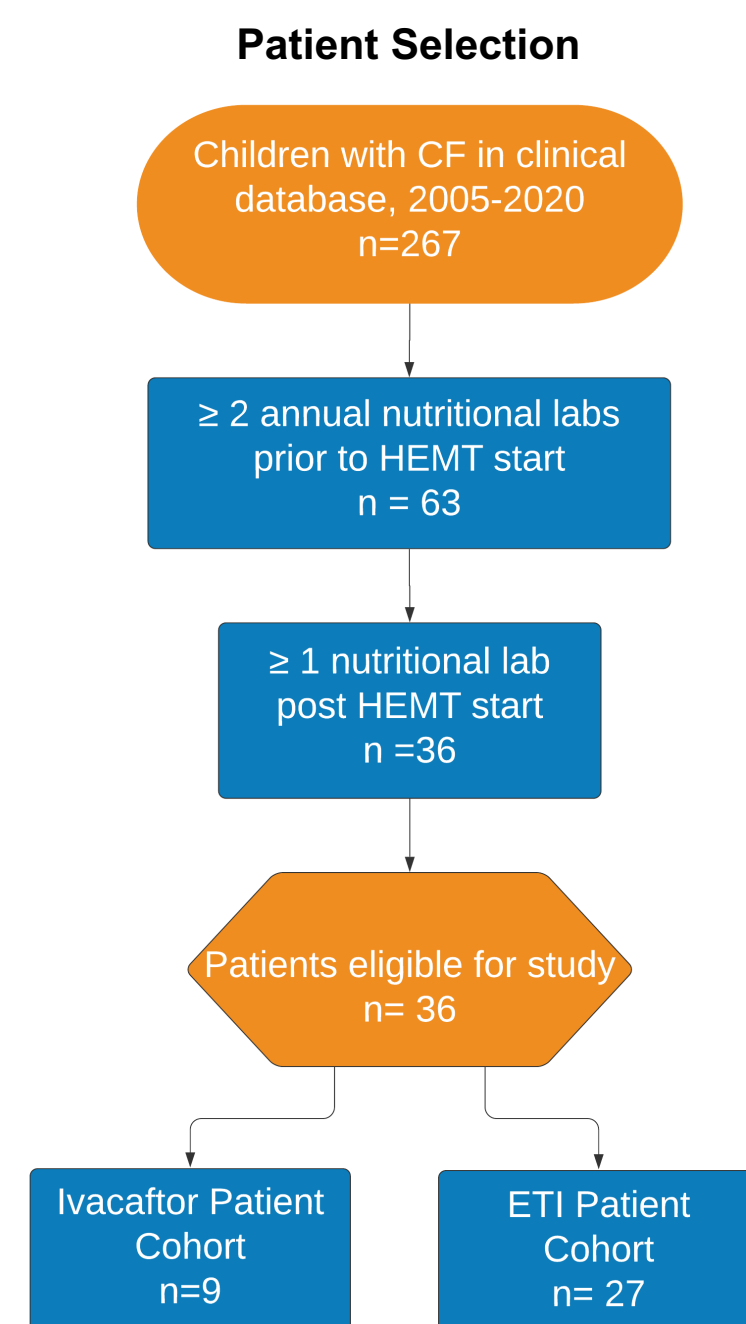


Table 2. Vitamin measurements before and after modulator initiation

	Ivacaftor (N=9)	ETI (N = 27)	Total (N = 36)
Vitamin A, mcg/dl			
Pre	41 (9.8)	38 (6.5)	39 (7.4)
Post	48 (13.5)	45 (10.8)	46 (11.4)
P-value	0.05	<0.001	
Vitamin D, ng/ml			
Pre	40.8 (5.1)	35 (9.3)	36 (8.8)
Post	46.7 (18.1)	38.6 (16)	41.7 (16.7)
P-Value	0.50	0.39	
Vitamin E alpha, mcg/ml			
Pre	13.8 (4.4)	10.7 (2.9)	11.5 (3.6)
Post	12.2 (2.7)	9.2 (4.4)	9.9 (4.2)
P-Value	0.04	0.01	
BMI % predicted			
Pre	44 (31)	60 (20)	57 (24)
Post	48 (33)	68 (22)	63 (26)
P-value	0.46	0.008	
FEV₁ % predicted			
Pre	96 (11)	94 (16)	95 (15)
Post	99 (15)	102 (15)	102 (15)
P-value	0.18	0.42	

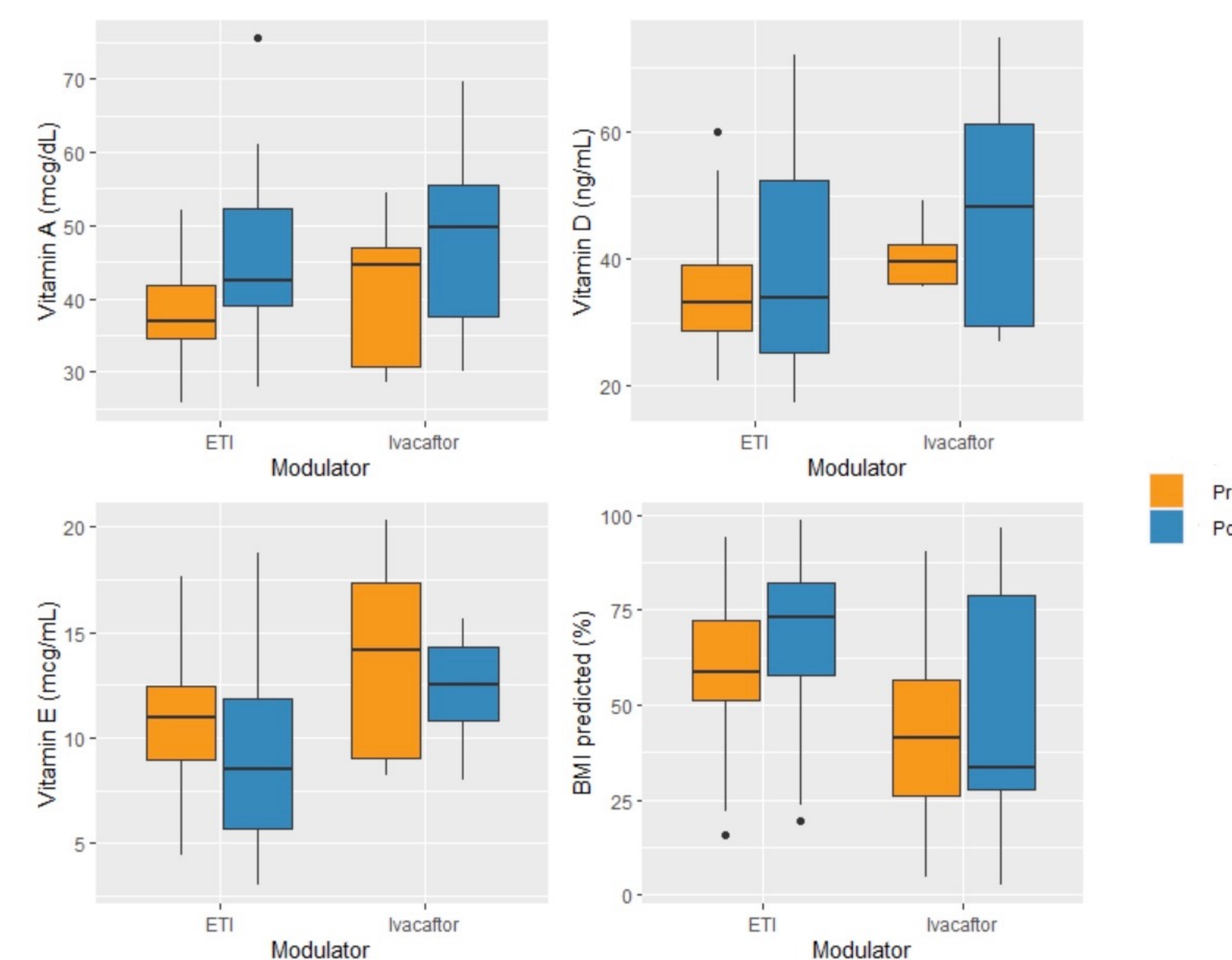
Values presented as mean (SD)

RESULTS

Table 1. Patient characteristics

	Ivacaftor (N=9)	ETI (N = 27)	Total (N = 36)
Age at modulator start, years	9.7 [6.6, 13.2]	13.4 [6.8, 21.7]	13.1 [6.6, 21.7]
Female sex	6 (67%)	12 (44%)	18 (50%)
Genotype risk group			
High	3 (33%)	25 (93%)	28 (78%)
Low	6 (67%)	2 (7%)	8 (22%)
Pancreatic status			
Insufficient	2 (22%)	27 (100%)	29 (81%)
Sufficient	7 (78%)	0 (0%)	7 (19%)
Number of vitamin measurements			
Pre	5 [3, 6]	7 [3, 10]	6 [3, 10]
Post	2 [1, 4]	2 [1, 6]	2 [1, 6]
Time range, years*			
Pre	0.03 to 9.3	0.01 to 12.2	0.10 to 12.2
Post	0.8 to 4.3	0.02 to 1.6	0.02 to 4.3

Continuous variables are summarized by median [min, max] and categorical variables are summarized using frequency with standard deviation
 *summarized using min and max



CONCLUSIONS

- Children treated with **ETI** had **higher vitamin A levels** following at least 3 months of treatment
- **Vitamin D** values did not change substantially, and **vitamin E** values were lower, although the change was unlikely to be clinically significant
- Vitamin levels **did not change** in those treated with **ivacaftor**, possibly due to small numbers, fewer pancreatic insufficient patients or less impact on fat absorption compared to ETI

IMPLICATIONS

- Treatment with **ETI** may improve **absorption of the fat-soluble vitamin A**
- Future studies with more participants and longer follow-up times may determine if changes in vitamin A levels persist and if **other fat-soluble vitamin** levels improve with time.
- Additional studies may evaluate if patients may decrease doses of fat soluble vitamin supplementation after starting ETI
- Factors such as **seasonal changes in vitamin D** values and supplementation should be considered in future studies

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