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MACFC MANCHESTER ADULT CYSTIC FIBROSIS CENTRE

NHS Manchester University NHS Foundation Trust

Elexacaftor /Tezacaftor/ Ivacaftor (ETI) - Nutritional benefits are greatest for those in greatest need

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BACKGROUND

Phase 3 trials with ETI reported an increase in weight and BMI in the short term. ETI became available to adults with CF in the United Kingdom in 2020.

AIM

To assess the impact of ETI on nutritional status at 12 months in a regional adult CF centre in the UK in an unselected clinical population

OBJECTIVES

1. To evaluate weight change and change in BMI at 12 months
2. To compare differences in impact of ETI on nutritional status based on sex, previous modulator use, enteral feeding, CFRD and CFRLD status and severity of disease at 12 months

METHODS

People commencing ETI had baseline demographic data collected and repeated at 12 months

Severity of lung disease was defined as severe FEV1<40%, moderate 40-79% and mild >80%

Body Mass Index (BMI) was used as a marker of nutritional status: underweight BMI of <18.5kg/m2, healthy weight BMI of 18.5-24.9kg/m2, overweight BMI of 25-29.9kg/m2 and obese > 30kg/m2

Relative weight gain is the percentage change from baseline to 12 months

Inclusion criteria: patient starting on ETI in 2020 with weight at baseline and at 12 months

Exclusion criteria: pregnancy, poor compliance, transferred to different centre or stopped due to side effects, no weight at 12 months

RESULTS

268 patients started on ETI during 2020 (note only F/F and F/MF genotypes included at this time)

- 16 were excluded due to pregnancy, poor compliance, transferred to different centre or stopped due to side effects
- 252 included in analysis

There was a significant increase in weight from 64.1 + 12.7kg to 68.2 +13.5kg, (p<0.001)

Mean relative weight gain of 6.8 + 7.7%

Absolute weight gain of 4.2kg + 4.6kg

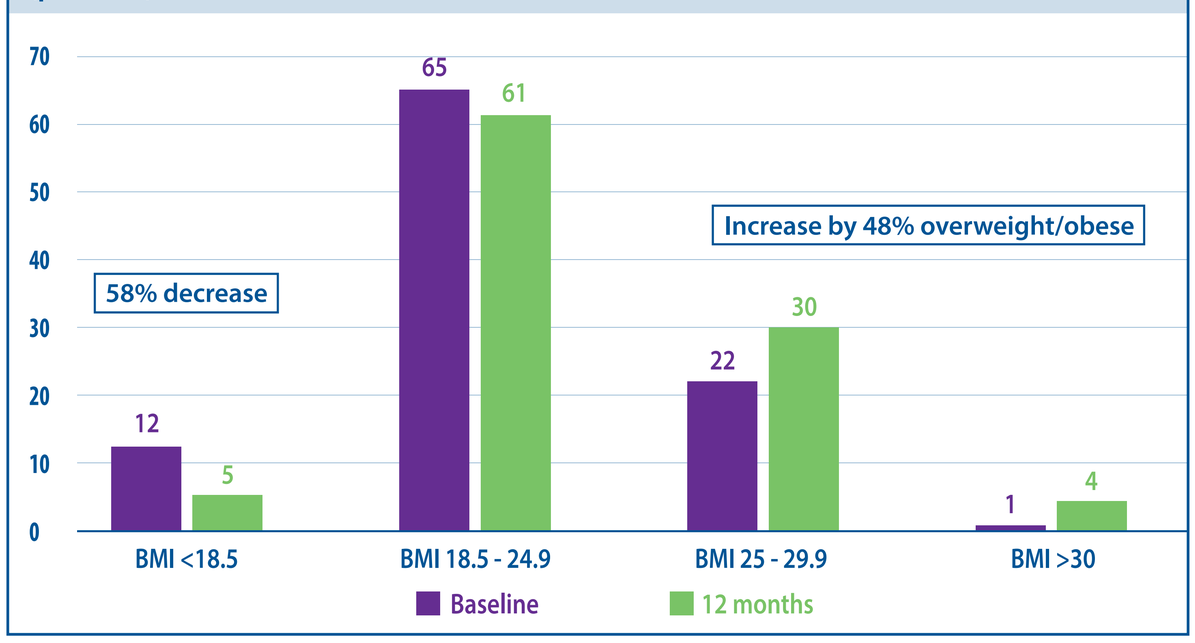
BMI increase of 1.45 + 1.61kg/m2

There is a significant inverse correlation between relative weight gain and baseline weight (r2 = -0.194, p=0.002)

There was no difference in weight gain according to previous modulator use (yes/no) or enteral feeding

Variable		Absolute Weight Gain		Relative Weight Gain		BMI Change	
Gender	Male (n=166) Female (n=86)	4.7 ± 4.7 kg 3.2 ± 4.3 kg	P = 0.016	7.2 ± 7.3% 6.0 ± 8.2%	P = 0.211	1.6 ± 1.6 kg/m² 1.2 ± 1.7 kg/m²	P = 0.128
CRFD status	CFRD (n=126) No CFRD (n=126)	3.8 ± 4.3 kg 4.6 ± 4.9 kg	P=0.155	6.5 ± 7.4% 7.1 ± 8.0%	P=0.482	1.3 ± 1.5 kg/m² 1.6 ± 1.7 kg/m²	P=0.288
CF Liver Disease	CFLD (n=77) No CFLD (n=175)	4.4 ± 5.2 kg 4.1 ± 4.3 kg	P=0.638	7.2 ± 8.4% 6.6 ± 7.3%	P=0.582	1.5 ± 1.8 kg/m² 1.4 ± 1.5 kg/m²	P=0.773
Baseline lung function	Grp 1: FEV_1 >80%pred(n=37) Grp 2: FEV_1 40-79% pred (n=129) Grp 3: FEV_1 <40% pred (n=71)	4.7 ± 4.5 kg 3.4 ± 4.2 kg 5.4 ± 4.9 kg*	P=0.008 *p=0.003 vs Grp 2	7.3 ± 7.2% 5.1 ± 6.6% 9.6 ± 8.6%	P=0.001 *p<0.001 vs Grp 2	1.6 ± 1.6 kg/m² 1.1 ± 1.4 kg/m² 1.9 ± 1.7 kg/m²	P=0.002 *p=0.001 vs Grp 2
Nutritional Status	Grp 1: BMI <18.5kg/m² (n30) Grp 2: BMI 18.5-24.9kg/m² (n=164) Grp 3: BMI 25-29.9kg/m² (n=55) Grp 4: 30kg/m² and above (n=3)	5.1 ± 5.0 kg 4.3 ± 4.6 kg 3.0 ± 4.3 kg 9.5 ± 2.6 kg	P=0.026	10.9 ± 10.5% 7.0 ± 7.3% 3.8 ± 5.6% 9.7 ± 2.9%	P<0.001	1.9 ± 1.8 kg/m² 1.5 ± 1.6 kg/m² 1.0 ± 1.5 kg/m² 3.2 ± 1.0 kg/m²	P=0.019

There was a significant change in the distribution of patients across BMI categories (p<0.001)



Baseline Status	Number at baseline	12 month Outcome
Underweight BMI	N=30 (12%)	Underweight n=10 (33%) Healthy BMI n=20 (67%)
Healthy BMI	N=164 (65%)	Underweight n=2 (1%) Healthy BMI n=127 (77%) Overweight n=34 (21%) Obese n=1 (1%)
Overweight BMI	N=55 (22%)	Normal weight n=7 (13%) Overweight n=42 (76%) Obese n=6 (11%)
Obese	N=3 (1%)	Obese n=3 (100%)

CONCLUSIONS

- Weight gain occurs in the overall population of people with CF on ETI, but is most marked in those underweight or with severe lung disease at baseline
- A changing nutritional demographic is now evident in adults with CF treated with ETI, with an increasing number of patients with CF becoming overweight or obese and less being underweight

Implications for future research and clinical services:

- Research and clinical services will need to focus on understanding the implications of this weight gain on prognosis and long term health
- CF services will need to adapt to these changing parameters and further longitudinal monitoring is essential to ensure that 'healthy' weight is maintained

References

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