



THIRTY-MONTH REAL-WORLD IMPACT OF ELEXACAFTOR/TEZACAFTOR/IVACAFTOR ON PULMONARY, NUTRITIONAL AND METABOLIC OUTCOMES IN CYSTIC FIBROSIS

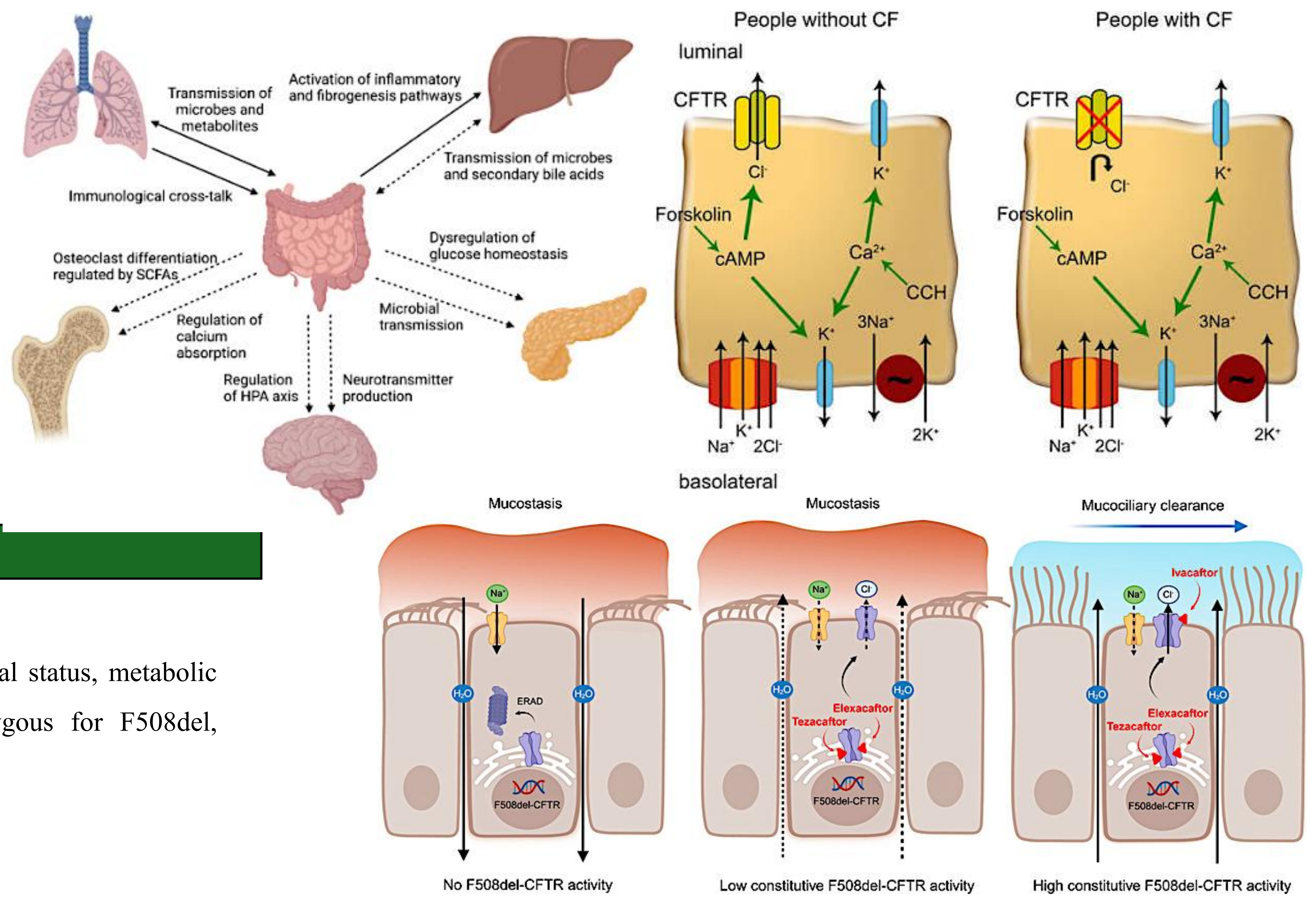
N. PERROTTA¹, L.A. FIORITO¹, A. VIRGILIO¹, G. AMATO¹, C. SERVIDIO¹, A. COLUCCIA¹, G. CIMINO².

¹ POLICLINICO UMBERTO I UNIVERSITY HOSPITAL, PHARMACY UNIT, ROME, ITALY.

² POLICLINICO UMBERTO I UNIVERSITY HOSPITAL, REGIONAL CYSTIC FIBROSIS CENTER, ROME, ITALY

BACKGROUND AND IMPORTANCE

Cystic fibrosis (CF) is a multisystem disease associated with malnutrition, chronic inflammation, and progressive lung decline. Elexacaftor/tezacaftor/ivacaftor (ETI) has transformed disease management, yet long-term effects on nutrition, metabolism, and liver health in homogeneous cohorts remain underexplored.



AIM AND OBJECTIVES

To evaluate the 30-month impact of ETI on pulmonary function, nutritional status, metabolic profile, inflammation, and hepatic safety in patients with CF homozygous for F508del, highlighting clinical benefits and emerging risks.

MATERIAL AND METHODS

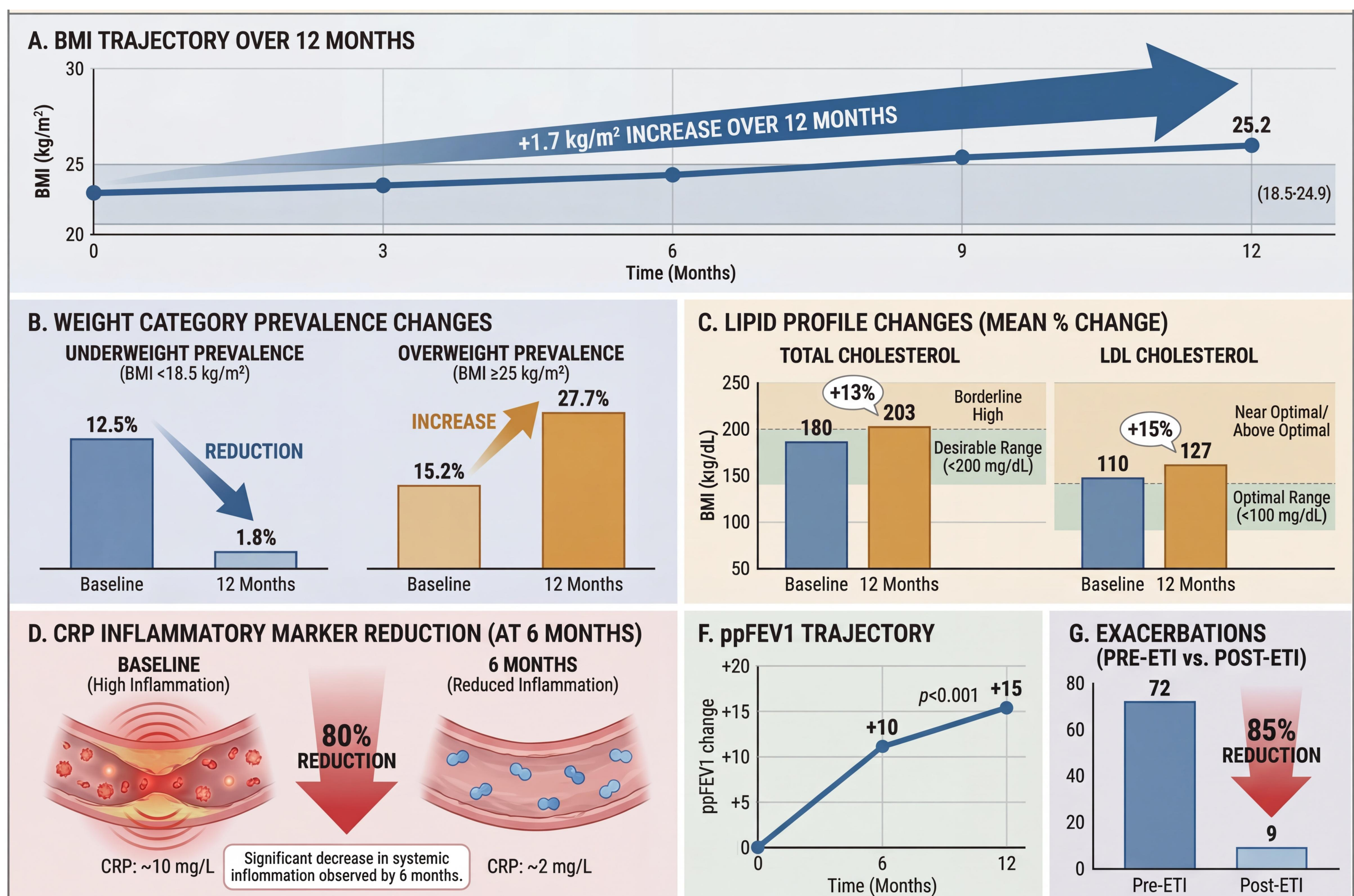
A retrospective, single-center cohort study was conducted at a Regional Reference CF Center. Patients >12 years, who initiated ETI between July 2021 and December 2024 were included. Clinical, spirometric, and biochemical data were collected at baseline and 6, 12, 24, and 30 months. Outcomes included lung function (ppFEV1), BMI, inflammatory markers, lipid profile, glycemic status, fat-soluble vitamins, liver function, and pulmonary exacerbations (12 months pre- and post-ETI). Longitudinal changes were analyzed using Friedman tests with post-hoc comparisons; subgroup differences were assessed with Mann-Whitney U tests.

RESULTS

112 patients (49% female, median age 31 years) were included; 83 were modulator-naïve and 29 pre-treated. ETI led to rapid and sustained pulmonary improvement: mean ppFEV1 increased by +10 points at 6 months and stabilized around +15 points above baseline through 30 months ($p < 0.001$). Exacerbations declined by 85% post-ETI (72 vs 9 events).

Nutritional status improved markedly: BMI increased by +1.7 kg/m² in the first year ($p < 0.001$), with underweight prevalence dropping from 12.5% to 1.8%, while overweight rose from 15.2% to 27.7%. Adolescents showed significant weight-for-age Z-score gains.

Lipids increased (total cholesterol +13%, LDL+15%) but remained within normal ranges; triglycerides, HDL, and glycemic control remained stable, with no new diabetes cases. Vitamin D levels improved. CRP fell by 80% at 6 months and remained reduced. Liver enzymes showed transient mild elevations in <5% of patients, with no fibrosis progression.



CONCLUSION AND RELEVANCE

ETI provides durable multisystem benefits, improving lung function, nutrition, and systemic inflammation while maintaining a favorable safety profile. However, the shift toward overweight/obesity and modest rises in cholesterol highlight evolving cardiometabolic risks. These findings support early ETI initiation and reinforce the need for updated CF care strategies including nutritional counselling, metabolic monitoring, and liver surveillance to mitigate long-term complications.