Title	***16.*** ***A PHASE 3 EFFICACY AND SAFETY STUDY OF ATALUREN (PTC124) IN PATIENTS WITH NONSENSE MUTATION CYSTIC FIBROSIS (PTC124-GD-021-CF)***
Project Coordinator	C. Braggion, MD (c.braggion@meyer.it), PI and partner of CTN
Internal Collaborators	Anna Silvia Neri, MD Michela Francalanci, Biologist, as study coordinator
Study design	A phase 3, randomized, controlled and parallel study to evaluate efficacy and safety of ataluren. EudraCT Number 2013-004581-34
Grant by	PTC Therapeutics, Inc.
Background and aims	In ~10% of patients with CF, the causative defect in the CFTR gene is a nonsense mutation that truncates CFTR protein production by introducing a premature stop codon into the CFTR messenger ribonucleic acid (mRNA). Ataluren is a novel, orally bioavailable, small-molecule drug that promotes ribosomal readthrough of mRNA containing a premature stop codon. Through this mechanism of action, ataluren has the potential to overcome the genetic defect in patients for whom a nonsense mutation causes CF. Previous studies showed that Ataluren improved lung function (FEV1) in patients, which did not inhale tobramycin, and was generally well tolerated. The primary objective of this study is to evaluate the ability of ataluren to improve pulmonary function relative to placebo, as assessed by FEV1. Safety, the frequency of CF pulmonary exacerbations, quality of life, body weight will be the secondary objectives.
Inclusion criteria	Age ≥6 years; presence of a nonsense mutation in at least 1 allele of the CFTR gene; FEV1 ≥40% and ≤90% of predicted for age, gender, and height; resting oxygen saturation, as measured by pulse oximetry, ≥92% on room air; screening laboratory values within the central laboratory ranges specified in protocol.
Exclusion criteria	Known hypersensitivity to any of the ingredients or excipients of the study drug; previous participation in the Phase 3 trial of Ataluren; any change in a chronic treatment/prophylaxis regimen for CF or pulmonary exacerbation within 4 weeks prior to screening; chronic use of inhaled aminoglycosides (eg, tobramycin) or use of inhaled aminoglycosides within 4 months prior to screening; history of solid organ or hematological transplantation; major complications of lung disease within 8 weeks prior to screening; known portal hypertension; positive hepatitis B surface antigen, hepatitis C antibody test, or human immunodeficiency virus (HIV) test; pregnancy or breast-feeding; current smoker or a smoking history.
Methods	Treatment will comprise continuous daily treatment with oral ataluren administered 3 times per day or placebo for 48 weeks. Visits will be performed every ~8 weeks up to 4 weeks after the end of treatment. Physical exams, vital signs, weight, BMI, spirometry and ECG will be performed at each visit. Blood and urine samples will be collected and questionnaire for quality of life will be administred at each visit. A renal ultrasound will be performed at the beginning and at the end of study and during the study if necessary.
Expected results and anticipated output	The objective of the study is to evaluate efficacy and safety of long term treatment with Ataluren.
Start of recruitment	February 2015
End of experimental plan	After 48 weeks of study drug treatment
Pubblication on medical Journal	