Title	***19.*** ***A phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety and tolerability of CTX-4430 administered orally once a day for 48 weeks in adults with cystici fibrosis (CTX-4430-CF-201)***
Project Coordinator	C. Braggion, MD (c.braggion@meyer.it), PI and member of CTN
Internal Collaborators	Maria Chiara Cavicchi MD Michela Francalanci, Biologist, study coordinator
Study design	This is a phase 2, double-blind, randomized, placebo-controlled study. A total of 195 CF patients will be randomized to receive 50 mg CTX-4430, 100 mg CTX-4430, or placebo in a 1:1:1 ratio. EudraCT Number 2015-002677-38
Grant by	Celtaxsys, Inc.
Background and aims	Cystic fibrosis (CF) pathology is characterized by a cycle of infection, inflammation and airway obstruction. Leukotriene a4 hydrolase (LTA4H) is an enzyme, which catalyzes the formation of the ultimate pro-inflammatory mediator leukotriene B4 (LTB4) from LTA4. LTB4 is a powerful attractant and activator of inflammatory immune cells, particularly neutrophils. CF lung disease is characterized by significant neutrophilic infiltrates in the small airways and elevation of LTB4 in the airways. In destructive pulmonary diseases such as CF, inhibition of LTB4 production has the potential to reduce both neutrophil influx and release of damaging neutrophil-derived enzymes such as elastase. The involvement of neutrophils and critical role of LTB4 suggests that inhibition of LTA4H is reasonable potential target for further clinical evaluation. CTX-4430 is a novel synthetic, small-molecule, LTA4H inhibitor and has also shown inhibition of LTB4 production after administration in both animal and human studies.
Inclusion criteria	18 to 30 years of age; medically stable with stable regimen of CF treatments; at least 1 pulmonary exacerbation in the 12 months before screening; FEV1>o= 50% predicted; resting oxygen saturation>92%; BMI>o=17.0 kg/m2; no use of tobacco or nicotine; females must agree to use a highly effective contraception method.
Exclusion criteria	History of organ transplantation; clinically significant hemoptysis; positive sputum culture for Burkholderia cepacia complex or Mycobacterium abscessus; ABPA; abnormal liver function; clinically unstable.
Methods	The study drug will be administered once a day orally for 48 weeks of treatment. Visits will be conducted approximately every 4 weeks from start to follow-up visit (4 weeks after the end of treatment). During each visit will be performed physical exam, spirometry and ECG; a blood sample and urine sample will be collected for routine measurements and for pharmacokinetic (PK) analysis and a questionnaire for quality of life will be administered. Sputum will be induced and a sample collected before the first dose and after 8, 24 and 48 weeks.
Expected results and anticipated output	Safety and tolerability of CTX-4430 administered orally once-daily for 48 weeks
Start of recruitment	September 2016
End of experimental plan	After 48 weeks of study drug treatment
Pubblication on medical Journal	