Title	***15.*** ***A Phase 3, Rollover Study to Evaluate the Safety and Efficacy of Long-term Treatment With Lumacaftor in Combination With Ivacaftor in Subjects Aged 12 Years and Older With Cystic Fibrosis, Homozygous or Heterozygous for the F508del-CFTR Mutation (VX-105)***
Project Coordinator	C. Braggion, MD (c.braggion@meyer.it), PI, Partner of CTN
Internal Collaborators	Anna Silvia Neri, MD Michela Francalanci, Biologist, as study coordinator
Study design	Phase 3, parallel-group, multicenter rollover study in subjects with CF who are homozygous or heterozygous for the F508del-CFTR mutation and who participated in study 103, study 104, or cohort 4 of study 102. Study 105 is designed to evaluate the safety and efficacy of long-term treatment of lumacaftor in combination with ivacaftor. (Eudract no. *2013-000604-41*).
Grant by	Vertex
Background and aims	The *F508del-CFTR* mutation interferes with the ability of the CFTR protein to reach and remain at the cell surface, as well as to open and close, resulting in decreased Cl^- transport. The combined effect is a marked reduction in F508del-CFTR-mediated Cl^- secretion that impairs fluid regulation and promotes accumulation of thick, sticky mucus in the airway. The corrector Lumacaftor should modify the cellular processing and delivery of CFTR protein to the cell surface. The potentiator Ivacaftor should increase channel gating activity of CFTR protein at the cell surface to enhance ion transport. A modest restoration of Cl^- secretion through the action of a potentiator and/or corrector could provide adequate airway hydration and so alleviate the cycle of mucus plugging, airway infection and inflammation.
Inclusion criteria	Subjects who completed 24 weeks of study drug treatment in study 103 or study 104
Exclusion criteria	History of any comorbidity or laboratory abnormality; pregnant and nursing females; sexually active subjects of reproductive potential who are not willing to follow the contraception requirements; history of drug intolerance in the prior study; history of poor compliance with study drug and/or procedures in the previous study.
Methods	The duration of the study will be about 2 years. Subjects will receive 1 of 2 treatments during treatment Period (Day 1 through Week 96) as follows: **Treatment Arm 1:** 600 mg lumacaftor once daily + 250 mg ivacaftor every 12 hours (administered orally) **Treatment Arm 2:** 400 mg lumacaftor every 12 hours + 250 mg ivacaftor every 12 hours (administered orally) A Safety Follow-up Visit is scheduled 4 weeks after the Week 96 Visit. Visits will be organized every three months with the same exams and measurements of study 103 (physical examination, vital signs, weight, BMI, spirometry, ECG and administration of CFQ-R questionaire).
Expected results and anticipated output	To evaluate the long term safety and tolerability of lumacaftor in combination with ivacaftor in subjects with cystic fibrosis (CF) who are homozygous for the *F508del-CFTR* mutation.
Start of recruitment	March 2014
End of experimental plan	After 96 weeks of study drug treatment
Pubblication on medical Journal	