Title	***8.*** ***A randomized, double-blind, placebo-controlled parallel group study to confirm the efficacy and the safety of tiotropium 5 µg administered once daily via the Respimat® device for 12 weeks in patients with cystic fibrosis***
Project Coordinator	C. Braggion, MD (c.braggion@meyer.it)
Internal Collaborators	R. Pasotto, biologist (study coordinator and data manager)
Study design	Phase III, multicentric study, which involve different countries in Europe and include the CTN* (our Center will coordinate 3 Centres in Italy)(Eudract no. 2010-019802-17) *: Clinical Trial Network of the European Cystic Fibrosis Network, which include 18 European Centres (3 from Italy)
Grant by	Boehringer Ingelheim
Background and aims	Approximately 80% of patients with cystic fibrosis (CF) use short- and/or long-acting bronchodilators although their use as a therapy is not clearly defined. The available evidence indicates that bronchodilator agents in general are able to improve pulmonary function and lessen wheezing in many patients with CF. The approximately equal effectiveness of β2-agonists and vagal efferent blocking agents suggests that much of the airway obstruction in CF is parasympathetically mediated. It is, therefore reasonable to conclude that anticholinergics could make an important contribution to reversing airway obstruction. Tiotropium is developed as a long-acting anticholinergic bronchodilator for treatment of bronchospasm and dyspnea in patients with chronic obstructive pulmonary disease (COPD). It is two to four-fold more potent than ipratropium bromide and its duration of action exceeds 24 hours compared to 6 hours for ipratropium bromide. The aim of this study is to evaluate the effects of 12-week treatment with tiotropium bromide 5 µg q.d. compared to placebo administered via the Respimat® device on lung function in patients with CF.
Inclusion criteria	Male or female patients with CF, able to perform spirometry and with a FEV_1 value > 25% of predicted value; patients must be clinically stable (no evidence of pulmonary exacerbation within 4 weeks of screening and pre-bronchodilator FEV_1 at Visit 2 within 15% of FEV_1 at Visit 1).
Exclusion criteria	Known hypersensitivity to study drug; participation in another study within 1 month; female patients who are pregnant or lactating and female patients of child bearing potential who are not using a medically approved form of contraception; start of a new chronic medication for CF within four weeks of screening; clinically significant disease or medical condition other than CF or CF-related conditions.
Methods	This is a 12-week, multi-dose, multi-center, multi-national, randomized, double-blind, placebo-controlled parallel group study followed by an open active treatment period of 13 months. The efficacy end-points are the percentual variation of FEV_1, FVC and FEF_{25-75} 30 minutes before and 60, 120, 180, 240 minutes after the drug inhalation, the number of pulmonary exacerbations and the change in the CFQ and RSSQ questionnaire items. The safety end-points are physical exam, vital signs, clinical laboratory tests (chemistry, haemathology), vital status, reported adverse events. Drug (5 µg q.d.: 2 actuation of 2,5 µg) and placebo will be inhaled via the Respimat device.
Expected results and anticipated output	To confirm the efficacy of 5 µg of tiotropium bromide identified in the phase II study.
Start of recruitment	For our Centre at 08.02.2011.
End of experimental plan	For our Centre and for adults at July 2011, for adolescents at August 2011.
Pubblication on medical Journal	4 adults patients and 3 children 9-11 yrs old have been recluted.