Title	***10.*** ***A single arm, open-label, multicenter, Phase IV trial to assess long term safety of tobramycin inhalation powder (TIP) in patients with Cystic Fibrosis***
Project Coordinator	C. Braggion, MD (c.braggion@meyer.it)
Internal Collaborators	V. Galici, MD (co-investigator), R. Pasotto (study coordinator), nurses, chest physiotherapists, lab technician
Study design	Phase IV, open label, single arm multicentric study, which involve different countries in Europe and include 5 Centres in Italy (Eudract no. 2011-0062000-32)
Grant by	Novartis Farma S.p.A.
Background and aims	Tobramycin belongs to the aminoglycoside class of antibiotics. TBM100 28 mg inhalation powder, hard capsules are a dry-powder formulation of tobramycin to be administered by a single dose dry-powder inhaler (T-326 Inhaler). The recommended administration scheme of TIP is similar to that of the established TOBI (300mg/5mL tobramycin inhalation solution) regimen: repeated cycles of 28 days on-drug twice daily, followed by 28 days off-drug period. TIP is designed to provide the same level of efficacy and safety as TOBI, but with a greatly simplified method of administration. This study is designed to provide safety data across 6 cycles in terms of: i) incidence of treatment emergent adverse events; ii) changing from baseline in *P. aeruginosa* tobramycin MIC; iii) clinical chemistry, hematology and audiology (will be performed at selected sites) and iV) to assess the efficacy of TIP over 6 cycles of treatment, as measured by the relative change in FEV_1 % predicted, FVC % predicted and FEF_{25-75} % predicted from baseline to the end of the dosing periods of each cycle.
Inclusion criteria	Male or female patients with CF ≥ 6 years of age, with FEV_1 at screening ≥ 25% and ≤ 75% of predicted value; documented positive lower respiratory tract culture for PA at the screening visit plus 1 documented positive lower respiratory tract cultures for PA within 6 months prior to screening visit; patients must be clinically stable.
Exclusion criteria	Patients with known hypersensitivity to aminoglycosides or inhaled antibiotics; use of inhaled/systemic anti-pseudomonal antibiotics within 28 days prior to study drug administration (Visit 2); female patients who are pregnant or lactating and female patients of potential child bearing who are not using 2 approved form of contraception; signs and symptoms of acute pulmonary disease; sputum culture or deep cough throat swab positive for Burkholderia cenocepacia complex within 2 years prior to screening and at screening (Visit 1); hemoptysis more than 60 mL at any time within 30 days prior to study drug administration (Visit 2); hearing loss or chronic tinnitus deemed clinically significant by the investigator; serum creatinine 2 mg/dl or more, BUN 40 ml/dl or more, or an abnormal urinalysis at screening.
Methods	This is an open label, single arm multicentric study in CF patients, aged 6 years and older, with FEV_1 in the range 25-75% predicted, who have a chronic pulmonary infection with PA. The study consists of a 14-28 days screening period to test/re-confirm the presence of PA, a baseline visit (Visit 2), followed by the treatment phase of 6 cycles. Each cycles consists of 28 days (4 capsules twice a day) on-treatment period followed by 28 days off-treatment period. Total duration of treatment is expected to be up to 48 weeks with a total of 14 visits: 9 site visits and 5 telephone calls. Patients will have a site visit at the end of each on-treatment period.
Expected results and anticipated output	To confirm long term safety and efficacy of TIP hard capsules 28 mg four times, twice a day.
Start of recruitment	For our Centre at April 2012.
End of experimental plan	For our Centre at April 2013.
Pubblication on medical Journal	2-3 patients (aged 6 years and older) will be enrolled.