Titolo:	A phase II, single-arm, multicenter study of full treatment-free remission in patients with chronic myeloid leukemia in chronic phase treated with nilotinib in first-line therapy who have achieved a sustained deep molecular response for at least 1 year: DANTE study
Patologia:	chronic myeloid leukemia
Tipo di Studio:	single-arm, multicenter study
Fase:	2
Principali criteri di inclusione:	Patients eligible for inclusion in this study must meet **all** the following criteria: 1. Male and female patients 18 years or older. 2. Diagnosis of chronic myeloid leukemia according to the World Health Organization. 3. Patients with CML-CP under first-line treatment with nilotinib at the approved daily dose of 300 mg BID mg for at least 3 calendar years. Note: At study entry, an ongoing treatment at a dose ≥400 mg per day is allowed. 4. Sustained DMR defined as ≥ MR 4.0 (BCR-ABL level ≤0.01% IS) in all of the last 4 BCR-ABL RQ-PCR assessments with a minimum interval between each assessment of 3 months and a maximum interval of 6 months. 5. Patient must meet the following laboratory values at the screening visit: • Absolute Neutrophil Count ≥1.0 x 109/L • Platelets ≥75 x 109/L • Hemoglobin (Hgb) ≥ 9 g/dL • Serum creatinine < 1.5 mg/dL • Aspartate transaminase (AST) ≤ 3.0 x Upper Limit of Normal (ULN) • Alanine transaminase (ALT) ≤ 3.0 x ULN • Serum lipase ≤ 2 x ULN 6. Patient has an Eastern Cooperative Oncology Group (ECOG) performance status 0-2. 7. Study subjects must be able to comply with study procedures and follow-up examinations
Principali criteri di esclusione:	1. Patients with known atypical transcript. 2. CML treatment resistant mutation(s) (T315I, E255K/V, Y253H, F359C/V) detected if testing was done in the past (there is no requirement to perform mutation testing at study entry if it was not done in the past). 3. Dose reductions/interruptions due to neutropenia or thrombocytopenia in the past 6 months. 4. Patient ever attempted to permanently discontinue nilotinib

	treatment. 5. Known impaired cardiac function including any one of the following: • Inability to determine QT interval on ECG • Complete left bundle branch block • Long QT syndrome or a known family history of long QT syndrome • History of or presence of clinically significant ventricular or atrial tachyarrhythmias • Clinically significant resting bradycardia • QTcF > 480 msec • History or clinical signs of myocardial infarction within 1 year prior to study entry • History of unstable angina within 1 year prior to study entry • Other clinically significant heart disease (e.g. uncontrolled congestive heart failure or uncontrolled hypertension) 6. Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol. 7. History of acute pancreatitis within 1 year prior to study entry or past medical history of chronic pancreatitis. 8. Known presence of a significant congenital or acquired bleeding disorder unrelated to cancer. 9. History of other active malignancy within 5 years prior to study entry except for previous or concomitant basal cell skin cancer, previous cervical carcinoma in situ treated curatively. 10. Patients who have not recovered from prior surgery. 11. Treatment with other investigational agents (defined as not used in accordance with the approved indication) within 4 weeks of Day 1. 12. Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drug (e.g. ulcerative disease, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, small bowel resection, or gastric bypass surgery). 13. Patients actively receiving therapy with strong CYP3A4 inhibitors and/or inducers, and the treatment cannot be either discontinued or switched to a different medication prior to study entry. 14. Patients actively receiving therapy with herbal medicines that are strong CYP3A4 inhibitors and/or inducers, and the treatment cannot be either discontinued or switched to a different medication prior to study entry. These herbal medicines may include Echinacea, (including E. purpurea, E. angustifolia and E. pallida), Piperine, Artemisinin, St. John's Wort, and Ginkgo. 15. Pregnant or nursing (lactating) women. 16. Women of childbearing potential, defined as all women physiologically capable of becoming pregnant, **unless** they are using highly effective methods of contraception during dosing and

	for at least 14 days after stopping medication. There is a limited amount of data on pregnancies in patients while attempting treatment-free remission (TFR). If pregnancy is planned during the TFR phase, the patient must be informed of a potential need to re-initiate treatment with nilotinib during pregnancy Highly effective contraception methods include: • Total abstinence (when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception. • Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy), total hysterectomy, or tubal ligation at least six weeks before taking study treatment. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment. • Male sterilization (at least 6 months prior to screening). The vasectomized male partner should be the sole partner for that subject. • Use of oral, injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS), or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception. In case of use of oral contraception, women should have been stable on the same pill for a minimum of 3 months before starting the study. Women are considered post-menopausal and not of childbearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (i.e. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy, or tubal ligation at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of childbearing potential
Sede e contatti	Novartis FARMA S.p.A.