KURZPROTOKOLL
AC220-A-U302

Öffentlicher Titel	Phase 3 Studie zu Quizartinib bei de novo AML mit FLT3-ITD Mutation
Wissenschaftl. Titel	A Phase 3, Double-Blind, Placebo-controlled Study of Quizartinib Administered in Combination With Induction and Consolidation Chemotherapy, and Administered as Maintenance Therapy in Subjects 18 to 75 Years Old With Newly Diagnosed FLT3-ITD (+) Acute Myeloid Leukemia
Kurztitel	AC220-A-U302
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase III
Erkrankung	Blut: Akute myeloische Leukämie (AML): Neu diagnostiziert / de novo
Einschlusskriterien	- Must be competent and able to comprehend, sign, and date an Ethics Committee (EC)- or Institutional Review Board (IRB)- approved Informed Consent Form (ICF) before performance of any study-specific procedures or tests - >=18 years or the minimum legal adult age (whichever is greater) and<=75 years (at Screening) - Newly diagnosed, morphologically documented primary AML or AML secondary to myelodysplastic syndrome or a myeloproliferative neoplasm, based on the World Health Organization (WHO) 2008 classification (at Screening);36 - Eastern Cooperative Oncology Group (ECOG) performance status 0-2 (see Appendix 17.6 for descriptions) (at the time the subject signs their first informed consent form); - Presence of FLT3-ITD activating mutation in bone marrow (allelic ratio of>=3% FLT3-ITD/total FLT3) (Section 6.1.2) - Subject is receiving standard “7+3" induction chemotherapy regimen as specified in the protocol (see Section 5.4.1 for required anthracycline and cytarabine doses) - Adequate renal function defined as: a) Creatinine clearance >50 mL/min, as calculated with the modified Cockcroft Gault equation (Appendix 17.9) - Adequate hepatic function defined as: a)Total serum bilirubin (TBL) <=1.5 × ULN; b)Serum alkaline phosphatase, aspartate transaminase (AST) and alanine transaminase (ALT)<=2.5 × ULN - Serum electrolytes within normal limits: potassium, calcium (total, or corrected for serum albumin in case of hypoalbuminemia) and magnesium. If outside of normal limits, subject will be eligible when electrolytes are corrected - If a woman of childbearing potential, must have a negative serum pregnancy test upon entry into this study and must be willing to use highly effective birth control (Appendix 17.2) upon enrollment, during the treatment period and for 6 months following the last dose of investigational drug or cytarabine, whichever is later. A woman is considered of childbearing potential following menarche and until becoming postmenopausal (no menstrual period for a minimum of 12 months) unless permanently sterile (undergone a hysterectomy, bilateral salpingectomy or bilateral oophorectomy) - If male, must be surgically sterile or willing to use highly effective birth control (Appendix 17.2) upon enrollment, during the treatment period, and for 6 months following the last dose of investigational drug or cytarabine, whichever is later
Ausschlusskriterien	- Diagnosis of acute promyelocytic leukemia (APL), French-American-British classification M3 or WHO classification of APL with translocation, t(15;17)(q22;q12), or BCR-ABL positive leukemia (ie, chronic myelogenous leukemia in blast crisis); subjects who undergo diagnostic workup for APL and treatment with ATRA, but who are found not to have APL, are eligible (treatment with ATRA must be discontinued before starting induction chemotherapy) - Diagnosis of AML secondary to prior chemotherapy or radiotherapy for other neoplasms

- Prior treatment for AML, except for the following allowances: a)Leukapheresis; b)Treatment for hyperleukocytosis with hydroxyurea; c)Cranial radiotherapy for central nervous system (CNS) leukostasis; d)Prophylactic intrathecal chemotherapy; e)Growth factor/cytokine support
- Prior treatment with quizartinib or other FLT3-ITD inhibitors
- Prior treatment with any investigational drug or device within 30 days prior to Randomization (within 2 weeks for investigational or approved immunotherapy) or currently participating in other investigational procedures
- History of known CNS leukemia, including cerebrospinal fluid positive for AML blasts; lumbar puncture is recommended for subjects with symptoms of CNS leukemia to rule out extramedullary CNS involvement
- History of other malignancies, except adequately treated non-melanoma skin cancer, curatively treated in-situ disease, or other solid tumors curatively treated with no evidence of disease for at least 2 years
- Uncontrolled or significant cardiovascular disease, including any of the following: a)Bradycardia of less than 50 beats per minute, unless the subject has a pacemaker b)QTcF interval >450 msec; c)Diagnosis of or suspicion of long QT syndrome (including family history of long QT syndrome); d)Systolic blood pressure>=180 mmHg or diastolic blood pressure>=110 mmHg; eHistory of clinically relevant ventricular arrhythmias (eg, ventricular tachycardia, ventricular fibrillation, or Torsade de Pointes); f)History of second (Mobitz II) or third degree heart block (subjects with pacemakers are eligible if they have no history of fainting or clinically relevant arrhythmias while using the pacemaker); g)History of uncontrolled angina pectoris or myocardial infarction within 6 months prior to Screening; h)History of New York Heart Association Class 3 or 4 heart failure; i)Known history of left ventricular ejection fraction (LVEF)<=45% or less than the institutional lower limit of normal; j)Complete left bundle branch block
- Active acute or chronic systemic fungal, bacterial, or viral infection not well controlled by antifungal, antibacterial or antiviral therapy
- Known active clinically relevant liver disease (eg, active hepatitis B, or active hepatitis C)
- Known history of human immunodeficiency virus (HIV). Subjects should be tested for HIV prior to Randomization if required by local regulations or EC
- History of hypersensitivity to any excipients in the quizartinib/placebo tablets
- Females who are pregnant or breastfeeding
- Otherwise considered inappropriate for the study by the Investigator

Alter	18 - 75 Jahre
Molekularer Marker	FLT3
Sponsor	Daiichi Sankyo, Inc.
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02668653 EudraCT 2015-004856-24