KURZPROTOKOLL
2215-CL-0301

Öffentlicher Titel	Phase III Studie zu ASP2215 bei rezidivierter oder refraktärer AML mit FLT3-Mutation
Wissenschaftl. Titel	A Phase 3 Open-label, Multicenter, Randomized Study of ASP2215 versus Salvage Chemotherapy in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML) with FLT3 Mutation
Kurztitel	2215-CL-0301
Studienart	multizentrisch, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig, kontrolliert
Studienphase	Phase III
Erkrankung	Blut: Akute myeloische Leukämie (AML): Rezidiviert/refraktär
Einschlusskriterien	- Institutional Review Board-/Independent Ethics Committee-approved written Informed Consent and privacy language as per national regulations (e.g., Health Insurance Portability and Accountability Act Authorization for United States sites) must be obtained from the subject or legally authorized representative prior to any study-related procedures (including withdrawal of prohibited medication, if applicable). - Subject is considered an adult according to local regulation at the time of signing informed consent - Subject has a diagnosis of primary AML or AML secondary to myelodysplastic syndrome (MDS) according to World Health Organization classification [Swerdlow et al, 2008] as determined by pathology review at the treating institution. - Subject is refractory to or relapsed after first-line AML therapy (with or without HSCT) (see definition of line of therapy in Appendix 12.6). - - Refractory to first-line AML therapy is defined as: - a) Subject did not achieve CR/CRi/CRp under initial therapy. A subject eligible for standard therapy must receive at least 1 cycle of an anthracycline containing induction block in standard dose for the selected induction regimen. A subject not eligible for standard therapy must have received at least 1 complete block of induction therapy seen as the optimum choice of therapy to induce remission for this subject as per investigator’s assessment. - - Untreated first hematologic relapse is defined as: - a) Subject must have achieved a CR/CRi/CRp (criteria as defined by [Cheson et al, 2003], see Section 5.3) with first line treatment and has hematologic relapse. - Subject is positive for FLT3 mutation in bone marrow or whole blood as determined by the central lab. In the investigator's opinion, a subject with rapidly proliferative disease and unable to wait for the central lab results can be enrolled based on a local test performed after completion of the last interventional treatment. Subjects can be enrolled from a local test result if they have any of the following FLT3 mutations: FLT3-ITD, FLT3-TKD/D835 or FLT3-TKD/I836. - Subject has an ECOG performance status <= 2. - Subject is eligible for preselected salvage chemotherapy according to investigator assessment. - Subject must meet the following criteria as indicated on the clinical laboratory tests: - - Serum aspartate aminotransferase and alanine aminotransferase <= 2.5 x upper limit of normal (ULN) - - Serum total bilirubin <=1.5 x ULN - - Serum creatinine <= 1.5 x ULN or an estimated glomerular filtration rate of > 50 mL/min as calculated by the Modification of Diet in Renal Disease equation. - Subject is suitable for oral administration of study drug. - Female subject must either: - - Be of non-childbearing potential:

- -> Postmenopausal (defined as at least 1 year without any menses) prior to screening, or documented as surgically sterile (at least 1 month prior to screening)
- -Or, if of childbearing potential,
- -> Agree not to try to become pregnant during the study and for 180 days after the final study drug administration
- -> And have a negative urine pregnancy test at screening
- -> And, if heterosexually active, agree to consistently use highly effective contraception per locally accepted standards in addition to a barrier method starting at screening and throughout the study period and for 180 days after the final study drug administration.
- Female subject must agree not to breastfeed at screening and throughout the study period and for 60 days after the final study drug administration.
- Female subject must not donate ova starting at screening and throughout the study period and for 180 days after the final study drug administration.
- Male subject and their female partners who are of childbearing potential must be using highly effective contraception per locally accepted standards in addition a barrier method)starting at screening and continue throughout the study period and for 120 days after the final study drug administration.
- Male subject must not donate sperm starting at screening and throughout the study period and for 120 days after the final study drug administration.
- Subject agrees not to participate in another interventional study while on treatment

Ausschlusskriterien

- Subject was diagnosed as acute promyelocytic leukemia.
- Subject has BCR-ABL-positive leukemia (chronic myelogenous leukemia in blast crisis).
- Subject has AML secondary to prior chemotherapy for other neoplasms (except for MDS).
- Subject is in second or later hematologic relapse or has received salvage therapy for refractory disease.
- Subject has clinically active central nervous system leukemia
- Subject has been diagnosed with another malignancy, unless diseasefree for at least 5 years. Subjects with treated nonmelanoma skin cancer, in situ carcinoma or cervical intraepithelial neoplasia, regardless of the disease-free duration, are eligible for this study if definitive treatment for the condition has been completed. Subjects with organconfined prostate cancer with no evidence of recurrent or progressive disease are eligible if hormonal therapy has been initiated or the malignancy has been surgically removed or treated with definitive radiotherapy.
- Subject has received prior treatment with ASP2215 or other FLT3 inhibitors (with the exception of sorafenib and midostaurin used in first-line therapy regimen as part of induction, consolidation and/or maintenance).
- Subject has clinically significant abnormality of coagulation profile, such as disseminated intravascular coagulation.
- Subject has had major surgery within 4 weeks prior to the first study dose.
- Subject has radiation therapy within 4 weeks prior to the first study dose.
- Subject has congestive heart failure New York Heart Association (NYHA) class 3 or 4 or subject with a history of congestive heart failure NYHA class 3 or 4 in the past, unless a screening echocardiogram performed within 1 month prior to study entry results in a left ventricular ejection fraction that is >= 45%.
- Subjects with mean of triplicate Fridericia-corrected QT interval (QTcF) > 450 ms at Screening based on central reading.
- Subjects with Long QT Syndrome at Screening.

	- Subjects with hypokalemia and hypomagnesemia at Screening (defined as values below lower limit of normal [LLN]). - Subject has an active uncontrolled infection. - Subject is known to have human immunodeficiency virus infection. - Subject has active hepatitis B or C or other active hepatic disorder. - Subject has any condition which, in the investigator's opinion, makes the subject unsuitable for study participation. - Subject has active clinically significant GVHD or is on treatment with systemic corticosteroids for GVHD. - Subject has an FLT3 mutation other than the following: FLT3-ITD, FLT3-TKD/D835 or FLT3-TKD/I836.
Alter	18 Jahre und älter
Molekularer Marker	FLT3
Sponsor	Astellas Pharma
Registrierung in anderen Studienregistern	EudraCT 2015-000140-42