KURZPROTOKOLL
M15-656

Öffentlicher Titel	Phase II Studie zu Venetoclax und Azacitidin bei Patienten mit de novo AML, die für die Standardinduktionstherapie ungeeignet sind
Wissenschaftl. Titel	A Randomized, Double-Blind, Placebo Controlled Phase 3 Study of Venetoclax in Combination With Azacitidine Versus Azacitidine in Treatment Naïve Subjects With Acute Myeloid Leukemia Who Are Ineligible for Standard Induction Therapy
Kurztitel	M15-656
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase III
Erkrankung	Blut: Akute myeloische Leukämie (AML): Neu diagnostiziert / de novo
Einschlusskriterien	- Participant must have confirmation of Acute Myeloid Leukemia (AML) by World Health Organization (WHO) criteria, previously untreated and be ineligible for treatment with a standard cytarabine and anthracycline induction regimen due age or comorbidities. - Participant must be >= 18 years of age. - Participant must have a projected life expectancy of at least 12 weeks. - Participant must be considered ineligible for induction therapy defined by the following: a) >= 75 years of age; or b) >= 18 to 74 years of age with at least one of the following comorbidities: i) Eastern Cooperative Oncology Group (ECOG) Performance Status of 2 or 3; ii) Cardiac history of Congestive Heart Failure (CHF) requiring treatment or Ejection Fraction <= 50% or chronic stable angina; iii) Diffusing capacity of the Lung for Carbon Monoxide (DLCO) <= 65% or Forced Expiratory Volume in 1 second (FEV1) <= 65%; iv) Creatinine clearance >= 30 mL/min to < 45 ml/min; v) Moderate hepatic impairment with total bilirubin > 1.5 to <= 3.0 × Upper Limit of Normal (ULN); vi) Any other comorbidity that the physician judges to be incompatible with intensive chemotherapy must be reviewed and approved by the AbbVie Therapeutic Medical Director during screening and before study enrollment. - Participant must have an ECOG Performance status: a) 0 to 2 for Participants >= 75 years of age; or b) 0 to 3 for Participants >= 18 to 74 years of age. - Participant must have adequate renal function as demonstrated by a creatinine >= 30 mL/min; calculated by the Cockroft Gault formula or measured by 24 hours urine collection. - Participant must have adequate liver function as demonstrated by: a) aspartate aminotransferase (AST) <= 3.0 x ULN*; b) alanine aminotransferase (ALT) <= 3.0 x ULN*; c) bilirubin <= 1.5 x ULN* * Unless considered to be due to leukemic organ involvement; d) Subjects who are < 75 years of age may have a bilirubin of <= 3.0 x ULN - Female participants must be either postmenopausal defined as: a) Age > 55 years with no menses for 12 or more months without an alternative medical cause; b) Age 55 years with no menses for 12 or more months without an alternative medical cause AND an FSH level > 40 IU/L; or c) Permanently surgical sterile (bilateral oophorectomy, bilateral salpingectomy or hysterectomy); or d) Women of Childbearing Potential (WOCBP) practicing at least one protocol specified method of birth control, starting at Study Day 1 through at least 90 days after the last dose of study drug. - Male Participants who are sexually active, must agree, from Study Day 1 through at least 90 days after the last dose of study drug, to practice the protocol specified contraception. Male subjects must agree to refrain from sperm donation from initial study drug administration through at least 90 days after the last dose of study drug.

- Female participants of childbearing potential must have negative results for pregnancy test performed: a) At Screening with a serum sample obtained within 14 days prior to the first study drug administration, and b) Prior to dosing with urine sample obtained on Cycle 1 Day 1, if it has been > 7 days since obtaining the serum pregnancy test results.
- Participant must voluntarily sign and date an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of any screening or study-specific procedures.

Ausschlusskriterien

- Participant has received treatment with the following: a) A hypomethylating agent, venetoclax and/or chemo therapeutic agent for Myelodysplastic syndrome (MDS); b) Chimeric Antigen Receptor (CAR)-T cell therapy; c) Experimental therapies for MDS or Acute Myeloid Leukemia (AML); d) Current participation in another research or observational study.
- Participant has history of myeloproliferative neoplasm (MPN) including myelofibrosis, essential thrombocythemia, polycythemia vera, chronic myeloid leukemia (CML) with or without BCR-ABL1 translocation and AML with BCR-ABL1 translocation.
- Participant has the following: Favorable risk cytogenetics such as t(8;21), inv(16) or t(16;16) or t(15;17) as per the National Comprehensive Cancer Network (NCCN) Guidelines Version 2, 2016 for Acute Myeloid Leukemia.
- Participant has acute promyelocytic leukemia
- Participant has known active central nervous system (CNS) involvement with AML.
- Participant has known HIV infection (due to potential drug-drug interactions between antiretroviral medications and venetoclax) HIV testing will be performed at Screening, only if required per local guidelines or institutional standards.
- Participant is known to be positive for hepatitis B or C infection [HCV Ab indicative of a previous or current infection; and/or positive HBs Ag or detected sensitivity on HBV DNA PCR test for HBc Ab and/or HBs Ab positivity] with the exception of those with an undetectable viral load within 3 months screening. (Hepatitis B or C testing is not required).
- Participant has received strong and/or moderate CYP3A inducers within 7 days prior to the initiation of study treatment; additional details as described in the protocol.
- Participant has consumed grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges) or Starfruit within 3 days prior to the initiation of study treatment.
- Participant has a cardiovascular disability status of New York Heart Association Class > 2. Class 2 is defined as cardiac disease in which patients are comfortable at rest but ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain.
- Participant has chronic respiratory disease that requires continuous oxygen, or significant history of renal, neurologic, psychiatric, endocrinologic, metabolic, immunologic, hepatic, cardiovascular disease, any other medical condition or known hypersensitivity to any of the study medications including excipients of azacitidine that in the opinion of the investigator would adversely affect his/her participating in this study.
- Participant has a malabsorption syndrome or other condition that precludes enteral route of administration.
- Participant exhibits evidence of other clinically significant uncontrolled systemic infection requiring therapy (viral, bacterial or fungal).
- Participant has a history of other malignancies within 2 years prior to study entry, with the exception of: a) Adequately treated in situ carcinoma of the cervix uteri or carcinoma in situ of breast; b) Basal cell carcinoma of the skin or localized squamous cell carcinoma of the skin; c) Previous malignancy confined and surgically resected (or treated with other modalities) with curative intent; requires discussion with TA MD.

	- Participant has a white blood cell count > 25 × 10^9/L. (Hydroxyurea or leukapheresis are permitted to meet this criterion.)
Alter	18 Jahre und älter
Prüfzentren	**Universitätsmedizin Frankfurt** (Geschlossen) Medizinische Klinik II, Hämatologie/Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Allg. Ansprechpartner der Abteilung Häma/Onko
Sponsor	AbbVie
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02993523 EudraCT 2016-001466-28