KURZPROTOKOLL
ASTX727-02

Öffentlicher Titel	Phase III Studie zu ASTX727 bei MDS, CMML oder AML
Wissenschaftl. Titel	A Phase 3, Randomized, Open-Label, Crossover Study of ASTX727 (Cedazuridine and Decitabine Fixed-Dose Combination) versus IV Decitabine in Subjects with Myelodysplastic Syndromes (MDS), Chronic Myelomonocytic Leukemia (CMML), and Acute Myeloid Leukemia (AML)
Kurztitel	ASTX727-02
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig
Studienphase	Phase III
Erkrankung	Blut: Myeloische Neoplasien/Dysplasien: Chronische myelomonozytäre Leukämie (CMML) Blut: Myeloische Neoplasien/Dysplasien: Myelodysplastische Syndrome (MDS) Blut: Akute myeloische Leukämie (AML): Neu diagnostiziert / de novo
Einschlusskriterien	- Able to understand and comply with the study procedures, understand the risks involved in the study, and provide written informed consent before the first study-specific procedure; specifically able to comply with the PK assessment schedule during the first 2 treatment cycles - Men or women >=18 years who are candidates to receive IV decitabine according to FDA or European Medicines Agency (EMA) approved indications: In North America: Participants with MDS previously treated or untreated with de novo or secondary MDS, including all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia [CMML]), and subjects with MDS International Prognostic Scoring System (IPSS) int-1, -2, or high-risk MDS. In Europe: Participants with de novo or secondary AML, as defined by the World Health Organization (WHO) criteria, who are not candidates for standard induction chemotherapy - Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1 - Adequate organ function defined as follows: Hepatic: Total or direct bilirubin <=2 × upper limit of normal (ULN); aspartate transaminase/serum glutamic oxaloacetic transaminase (AST/SGOT) and alanine transaminase/serum glutamic pyruvic transaminase (ALT/SGPT) <=2.5 × ULN. Renal: serum creatinine <=1.5 × ULN or calculated creatinine clearance or glomerular filtration rate >50 mL/min/1.73 m2 for subjects with creatinine levels above institutional normal - No major surgery within 30 days of first study treatment - Life expectancy of at least 3 months - Women of child-bearing potential must not be pregnant or breastfeeding and must have a negative pregnancy test at screening. Women of non-childbearing potential are those who have had a hysterectomy or bilateral oophorectomy, or who have completed menopause, defined as no menses for at least 1 year AND either age >=65 years or follicle-stimulating hormone levels in the menopausal range - Subjects and their partners with reproductive potential must agree to use effective contraceptive measures during the study and for 3 months after the last dose of study treatment. Effective contraception includes methods such as oral contraceptives or double-barrier method (eg, use of a condom AND diaphragm, with spermicide)
Ausschlusskriterien	- Prior treatment with more than 1 cycle of azacitidine or decitabine. Prior cytotoxic chemotherapy for AML except for hydroxyurea to control high white blood cell (WBC) counts - Hospitalization for more than 2 days for documented febrile neutropenia, pneumonia, sepsis, or systemic infection in the 30 days before screening - Treatment with any investigational drug or therapy within 2 weeks of study treatment, or 5 half-lives, whichever is longer, before the first dose of study treatment, or ongoing clinically significant adverse events (AEs) from previous treatment

- Cytotoxic chemotherapy or prior azacitidine or decitabine within 4 weeks of first dose of study treatment
- Concurrent MDS therapies, including lenalidomide, erythropoietin, cyclosporine/tacrolimus, granulocyte-colony stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor, etc. (Prior treatment with these agents is permitted, provided that completion is at least 1 week before the first dose of study treatment.)
- Poor medical risk because of other conditions such as uncontrolled systemic diseases, active uncontrolled infections, or comorbidities that may put the patient at risk of not being able to complete at least 2 cycles of treatment
- Known significant mental illness or other condition, such as active alcohol or other substance abuse or addiction, that in the opinion of the investigator predisposes the subject to high risk of noncompliance with the protocol
- Rapidly progressive or highly proliferative disease (total white blood cell count of >15 × 10^9/L) or other criteria that render the subject at high risk of requiring intensive cytotoxic chemotherapy within the next 3 months
- Life-threatening illness or severe organ system dysfunction, such as uncontrolled congestive heart failure or chronic obstructive pulmonary disease, or other reasons including laboratory abnormalities, which, in the investigator's opinion, could compromise the subject's safety, interfere with the absorption or metabolism of ASTX727, or compromise completion of the study or integrity of the study outcomes
- Prior malignancy, except for adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, prostate cancer or breast cancer under control with hormone therapy, or other cancer from which the subject has been disease free for at least 2 years

Alter	18 Jahre und älter
Prüfzentren	**Universitätsklinikum Gießen und Marburg, Standort Marburg** (Geschlossen) Hämatologie, Onkologie und Immunologie Baldingerstraße 35043 Marburg Nina Marschalek Tel: 06421 58 63546 Fax: 06421 58 62703 studien-onkologie@uni-marburg.de
Sponsor	Astex Pharmaceuticals, Inc.
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03306264 (primäres Register) EudraCT 2018-003395-12