KURZPROTOKOLL
ETAL-4

Öffentlicher Titel	Phase III Studie zu Panobinostat nach Stammzelltransplantation bei Hochrisiko-AML und -MDS
Wissenschaftl. Titel	European Intergroup Trial on panobinostat maintenance after HSCT for high-risk AML and MDS - A randomized, multicenter phase III study to assess the efficacy of panobinostat maintenance therapy vs. standard of care following allogeneic stem cell transplantation in patients with high-risk AML or MDS
Kurztitel	ETAL-4
Studienart	prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase III
Erkrankung	Blut: Myeloische Neoplasien/Dysplasien: Myelodysplastische Syndrome (MDS) Blut: Stammzelltransplantation: Allogene Stammzelltransplantation Blut: Akute myeloische Leukämie (AML): sonstige Studien für akute Leukämien
Einschlusskriterien	- 1. Eligibility criteria for registration prior to HSCT: - - Adult patients (18-70 years of age) - - AML (except acute promyelocytic leukemia with PML-RARA and AML with BCR-ABL1) according to WHO 2016 classification (Appendix 1) with high-risk features defined as one or more of the following criteria: - -> refractory to or relapsed after at least one cycle of standard chemotherapy - -> > 10% bone marrow blasts at day 14-21 of the first induction cycle - -> adverse risk according to ELN 2017 risk stratification by genetics (Appendix 2) regardless of stage - -> secondary to MDS or radio-/chemotherapy - -> MRD positive before HSCT based on flow cytometry or PCR - or - - MDS with excess blasts (MDS-EB) according to the WHO 2016 classification (Appendix 3), or high-risk or very high-risk according to IPSS-R (Appendix 4) - - First allogeneic HSCT scheduled within the next 4-6 weeks using one of the following donors, conditioning regimens (Appendix 5) and strategies for GvHD prophylaxis: - -> Matched sibling or matched unrelated donor (i.e. 10/10 or 9/10 HLA-matched) or haploidentical family donor - -> Conditioning regimens: - (1) Reduced-intensity conditioning: - -> Fludarabine/Melphalan - -> Fludarabine/Busulfan2 (FB2) - (2) Myeloablative conditioning: - -> Fludarabine/Busulfan4 (FB4) - -> Busulfan/Cyclophosphamide (BU/CY) - -> Fludarabine/TBI 8 Gy - -> Cyclophosphamide/TBI 12 Gy - (3) Fludarabine/Cyclophosphamide/TBI 2 Gy in combination with post-Tx cyclophosphamide (PT-CY) only - (4) Thiotepa/Busulfan/Fludarabine (TBF) in the context of an haploidentical HSCT only - (5) In case of active disease at HSCT, salvage chemotherapy prior to conditioning is permitted

- - Strategies for GvHD prophylaxis:
- - HLA-matched donors:
- -> CSA + MMF +/- ATG
- -> CSA + MTX +/- ATG
- -> PT-CY + CSA
- - Haploidentical donors:
- -> PT-CY + CSA + MMF
- - No history of significant cardiac disease and absence of active symptoms, otherwise documented left ventricular EF >= 40%
- - Written informed consent for registration
- 2. Enrollment after HSCT:
- - Adult patients with high-risk AML or MDS as defined above
- - First allogeneic HSCT performed within 30 - 65 days prior to enrollment
- - Eastern Cooperative Group (ECOG) performance status <= 2 (Appendix 6)
- - Complete hematologic remission or complete hematologic remission with incomplete recovery (see section 14.1) documented by bone marrow aspiration within 14 days prior to randomization
- - Laboratory test results maximum 14 days prior to randomization within the following ranges:
- -> Absolute neutrophil count >= 1.0 x 109/L

Ausschlusskriterien

- 1. Eligibility criteria for registration prior to HSCT:
- - Prior treatment with a DAC inhibitor
- - HIV or HCV antibody positivity
- - Psychiatric disorder that interferes with ability to understand the study and give informed consent, and/or impacts study participation or follow-up.
- - Female patients who are pregnant or breast feeding
- - History of another primary malignancy that is currently clinically significant or currently requires active intervention
- 2. Enrollment after HSCT:
- - Active acute GvHD grade III-IV according to modified Glucksberg criteria (Appendix 7)
- - Active acute GvHD grade II or chronic GvHD moderate/severe according to NIH criteria (Appendix 8) requiring systemic corticosteroids > 0.5 mg/kg body weight of methylprednisolone equivalent or combination immunosuppressive treatment
- - Uncontrolled or significant heart disease, including recent myocardiac infarction, cardiac failure (NYHA II-IV), unstable angina pectoris, or clinically significant bradycardia
- - Long QT syndrome
- - QTcF >=480 msec on screening ECG to be performed within 14 days prior to enrollment
- - Concurrent use of medications that have a relative risk of prolonging QT interval or of inducing Torsade de Pointes, if such treatment cannot be discontinued or switched to a different medication prior to the first dose of study drug (see Table 9).
- - Other concurrent severe and/or uncontrolled medical conditions (e.g., uncontrolled diabetes mellitus, chronic obstructive or chronic restrictive pulmonary disease including dyspnoea at rest from any cause) or history of serious organ dysfunction or disease involving the heart, kidney, or liver and/or seropositive HIV or HCV .

	- - Serious active infection - - CMV reactivation, which is not responsive to first-line valganciclovir or ganciclovir - - Impaired gastrointestinal (GI) function or GI disease that may significantly alter the absorption of oral panobinostat (e.g., ulcerative disease, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, obstruction, or stomach and/or small bowel resection).
Alter	18 - 70 Jahre
Sponsor	Universität Frankfurt
Förderer	Novartis Pharma
Registrierung in anderen Studienregistern	EudraCT 2017-000764-15
Links	Studiendokumente zum Download (roXtra) Zu den Ein- und Ausschlusskriterien