CHARITÉ

Comprehensive Cancer Center
Universitätstumorzentrum

Studientitel	**AMLSG 29-18 (HOVON 150)** **A Phase 3, Multicenter, Double-blind, Randomized, Placebo-controlled Study of Ivosidenib or Enasidenib in Combination With Induction Therapy and Consolidation Therapy Followed by Maintenance Therapy in Patients With Newly Diagnosed Acute Myeloid Leukemia or Myelodysplastic Syndrome With Excess Blasts-2, With an IDH1 or IDH2 Mutation, Respectively, Eligible for Intensive Chemotherapy.**	
EudraCT-Nummer	**2018-000451-41**	
ClinicalTrials.gov Identifier	**NCT03839771**	
Sponsor	HOVON Foundation	
Ansprechpartner*in	Prof. Dr. med. Jörg Westermann	
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Wichtigste Einschlusskriterien	• Age ≥18 years • Newly diagnosed AML or MDS-EB2 defined according to WHO criteria, with a documented IDH1 or IDH2 gene mutation (as determined by the clinical trial assay) at a specific site (IDH1 R132, IDH2 R140, IDH2 R172). AML may be secondary to prior hematological disorders, including MDS, and/or therapy-related (in which prior disease should have been documented to have existed for at least 3 months). Patients may have had previous treatment with hypomethylating agents (HMAs) for MDS. HMAs have to be stopped at least four weeks before registration • Patients with dual mutant FLT3 and IDH1 or IDH2 mutations may be enrolled only if, for medical or other reasons, treatment with a FLT3 inhibitor is not considered. • Considered to be eligible for intensive chemotherapy. • ECOG/WHO performance status ≤ 2 • Adequate hepatic function as evidenced by:	

	o Serum total bilirubin ≤ 2.5 × upper limit of normal (ULN) unless considered due to Gilbert's disease (e.g. a mutation in UGT1A1) (only for patients in IDH2 cohort), or leukemic involvement of the liver - following written approval by the (Co)Principal Investigator. o Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) ≤ 3.0 × ULN, unless considered due to leukemic involvement of the liver, following written approval by the Principal Investigator. • Adequate renal function as evidenced by creatinine clearance > 40 mL/min based on the Cockroft-Gault formula for glomerular filtration rate (GFR). • Able to understand and willing to sign an informed consent form (ICF). • Written informed consent Female patient must either: o Be of nonchildbearing potential: Postmenopausal (defined as at least 1 year without any menses) prior to screening, or Documented surgically sterile or status posthysterectomy (at least 1 month prior to screening) o Or, if of childbearing potential: Agree not to try to become pregnant during the study and for 6 months after the final study drug administration And have a negative urine or serum 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 6 months after the final study drug administration. • Highly effective forms of birth control include: o Consistent and correct usage of established hormonal contraceptives that inhibit ovulation, o Established intrauterine device (IUD) or intrauterine system (IUS), o Bilateral tubal occlusion, o Vasectomy (A vasectomy is a highly effective contraception method provided the absence of sperm has been confirmed. If not, an additional

	highly effective method of contraception should be used.) o Male is sterile due to a bilateral orchiectomy. o Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual activity during the entire period of risk associated with the study drug. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the patient. • List is not all inclusive. Prior to enrollment, the investigator is responsible for confirming patient will utilize highly effective forms of birth control per the requirements of the CTFG Guidance document 'Recommendations related to contraception and pregnancy testing in clinical trials', September 2014 (and any updates thereof) during the protocol defined period. o Female patient must agree not to breastfeed starting at screening and throughout the study period, and for 2 months and 1 week after the final study drug administration. o Female patient must not donate ova starting at screening and throughout the study period, and for 6 months after the final study drug administration. ▪ Male patient and their female partners who are of childbearing potential must be using highly effective contraception per locally accepted standards in addition to a barrier method starting at screening and continue throughout the study period and for 4 months and 1 week after the final study drug administration ▪ Male patient must not donate sperm starting at screening and throughout the study period and for 4 months and 1 week after the final study drug administration. ▪ Subject agrees not to participate in another interventional study while on treatment