CHARITÉ

Comprehensive Cancer Center
Universitätstumorzentrum

Studientitel	**AMLSG 28-18 (HOVON 156)** **A Phase 3, Multicenter, Open-label, Randomized, Study of Gilteritinib Versus Midostaurin in Combination With Induction and Consolidation Therapy Followed by One-year Maintenance in Patients With Newly Diagnosed Acute Myeloid Leukemia (AML) or Myelodysplastic Syndromes With Excess Blasts-2 (MDS-EB2) With FLT3 Mutations Eligible for Intensive Chemotherapy**	
EudraCT-Nummer	**2018-000624-33**	
ClinicalTrials.gov Identifier	**NCT04027309**	
Sponsor	HOVON Foundation	
Ansprechpartner*in	Prof. Dr. med. Jörg Westermann	
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Wichtigste Einschlusskriterien	• Age ≥18 years • Newly diagnosed AML or MDS with excess of blasts-2 (EB2) defined according to WHO criteria (appendix A), with centrally documented FLT3 gene mutation (either TKD or ITD or both). AML may be secondary to prior hematological disorders, including MDS, and/or therapy-related. Patients may have had previous treatment with erythropoiesis stimulating agents (ESA) or hypomethylating agents (HMAs) for an antecedent phase of MDS. ESA and HMAs have to be stopped at least four weeks before registration. • FLT3 mutation as assessed by DNA fragment analysis PCR for FLT3-ITD and FLT3-TKD mutation. Positivity is defined as a FLT3-ITD or FLT3-TKD / FLT3-WT ratio of ≥ 0.05 (5%). • Considered to be eligible for intensive chemotherapy • Patient is suitable for oral administration of study drug • WHO/ECOG performance status ≤ 2	

	• Adequate hepatic function as evidenced by
	  o Serum total bilirubin ≤ 2.5 × upper limit of normal (ULN) unless considered due to leukemic involvement 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 following written approval by the (co) Principal Investigator
	• Adequate renal function as defined by creatinine clearance > 40 mL/min based on the Cockroft-Gault glomerular filtration rate (GFR)
	• Written informed consent
	• Patient is capable of giving 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:

	▪ Consistent and correct usage of established hormonal contraceptives that inhibit ovulation, ▪ Established intrauterine device (IUD) or intrauterine system (IUS), ▪ Bilateral tubal occlusion, ▪ 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.) ▪ Male is sterile due to a bilateral orchiectomy. ▪ 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. • Patient agrees not to participate in another interventional study while on treatment