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| **Scientific Title** | A phase I study of a combination of 5-azacitidine followed by lenalidomide in high-risk MDS RAEB or relapsed/refractory AML patients with cytogenetic abnormalities including –5 or del(5q) |
| **Short Title** | AZALE |
| **Id KN/ELN** | LN_DEUTSC_2008_419 |
| **Trialgoup** | Deutsche MDS |
| **Type of Trial** | multicentric, single-group, open-label |
| **Phase** | Phase I |
| **Disease** | Myelodysplastic Syndrome( MDS) Intermedia II and high risk |
| **Stage of Disease** | . |

**Aim**

- Determine the maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of Revlimid® (lenalidomide) in combination with Vidaza® (5-azacitidine)
- Assess the response rate of patients to combination therapy with Revlimid® (lenalidomide) and Vidaza® (azacitidine), as defined by the International Working Group (IWG) criteria (see Appendix 02 for MDS and 03 for AML)
- Determine the safety profile of this regimen
- To assess biomarker modulation by this regimen (e.g. methylation)

**Outcomes**

- name Maximum tolerated dose (MTD) of Revlimid® in combination with Vidaza® during the first cycle (Primary Outcome)
- name Safety (type, frequency, severity, and relationship of adverse events to study treatment); Clinical and cytogenetic response, Modulation of biotargets including methylation

**Inclusion Criteria**

- Understand and voluntarily sign an informed consent form.
- Age >=18 years at the time of signing the informed consent form
- Able to adhere to the study visit schedule and other protocol requirements
- Relapsed or refractory (not responding to at least one cycle of induction chemotherapy1) AML (20% blasts, WHO classification) including therapy-related (t-)AML with karyotype abnormalities involving monosomy 5 or del(5q) or MDS and t-MDS RAEB according to WHO classification (RAEB-1 and RAEB-2) with a complex karyotype involving monosomy 5 or del(5q) either previously treated or untreated
- Not eligible for an immediate allogeneic HSCT (due to donor inavailability)
- All previous MDS or AML specific therapy with exception of corticosteroids not exceeding doses of 10mg/day prednisone must have been discontinued at least 1 week prior to study enrollment
- ECOG performance status of ? 3 at study entry (see Appendix 01).
- Laboratory test results within these ranges: Serum creatinine <= 2.0 mg/dL, Total bilirubin <= 3 x ULN, AST (SGOT) and ALT (SGPT) <= 3 x ULN
- Females of childbearing potential (FCBP)† must agree to use one reliable forms of contraception or to practice complete abstinence from heterosexual intercourse during the following time periods related to this study: for at least 28 days before starting study drug, while participating in the study and for at least 28 days after discontinuation from the study

**Exclusion Criteria**

- Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from signing the informed consent form
- Pregnant or breast feeding females. (Lactating females must agree not to breast feed while on study)
- Any condition, including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study or confounds the ability to interpret data from the stud

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| | - Known hypersensitivity to thalidomide, lenalidomide, 5-azacitidine or mannitol<br>- The development of erythema nodosum if characterized by a desquamating rash while taking thalidomide or similar drugs<br>- Known positive for HIV or acute infectious hepatitis, type A, B or C |
| **Age** | >= 18 years |
| **Status** | Closed |
| **start of Recruitment** | 30.10.2008 |
| **Target Sample Size** | 30 |
| **Leader** | Platzbecker, Prof. Dr. med., Uwe<br>Universitätsklinikum Dresden<br>Medizinische Klinik und Poliklinik<br>Fetscherstr. 74<br>01307 Dresden<br>Tel: +49 (0)351 4582583<br>Fax: +49 (0)351 458-5362<br>Email: Uwe.Platzbecker@uniklinikum-dresden.de |
| **Centre of Trial** | Universitätsklinikum Carl Gustav Carus, Dresden |
| **Diagnostics** | **DNA-Mythylation**<br>Genexpressionslabor der Med. Klinik III, Charité Universitätsmedizin Berlin, Campus Benjamin-Franklin<br>**gene expression**<br>Hämatologisches Labor, Universitätsklinikum Dresden |
| **Supporters** | Celgene |
| **Other Registers** | ClinicalTrials.govNCT00923234<br>European Clinical Trials Database - EUDRACT2008-005884-32 |