Public Title	Temsirolimus in Myelodysplastic Syndrome
Scientific Title	Treatment of MDS patients with single agent temsirolimus - a pilot study
Short Title	TEMDS
Id KN/ELN	LN_DEUTSC_2009_327
Trialgoup	Deutsche MDS
Type of Trial	multicentric, open-label, pilot study
Phase	N/A
Disease	Myelodysplastic Syndrome(MDS) Low risk and intermedia I Myelodysplastic Syndrome(MDS) Intermedia II and high risk
Stage of Disease	.
Aim	- Is to evaluate the response of MDS patients to temsirolimus. An overall response rate of 20 % or more according to modified IWG-criteria will be regarded as clinically significant. - • To describe the safety and tolerability of temsirolimus in MDS; - • to determine the effects of temsirolimus on quality of life in patients with MDS; - • to determine the effect of temsirolimus on modulating molecular targets in MDS targets
Outcomes	- Primary endpoint is the overall hematological response rate (combination of CR, PR, marrow-CR and SD with HI) at 4 months using modified IWG-criteria. (Primary Outcome) - Toxicity as measured by NCI CTCAE v3.0; - • overall survival at 1 year; - • progression-free survival at 1 year; - • rate of leukemic progression at 1 year; - • overall hematological response rate at 1 year using modified IWG-criteria; - • quality of life as measured by EORTC-QLQ30.
Inclusion Criteria	- •Age >=18 years at the time of signing the informed consent form; - • Patients able to understand the consequences of participating in this trial and not - - having any disorders or other circumstances (i.e. being in ward or imprisoned) which - - keeps them from giving written informed consent; - • cytologically or histologically established diagnosis of de novo or therapy-related MDS according to the FAB-classification, either previously treated or untreated, presenting with: - - Group I (low-risk): Low- or INT-1 risk with and without pretreatment - - or - - Group II (high-risk): INT-2 or HIGH-risk IPSS with 5-Azacytidine treatment failure - CMML patients of dysplastic phenotype (WBC < 13 Gpt/l) may be included in both arms according to IPSS. CMML patients showing proliferative phenotype (WBC >=13 Gpt/l) will be included in the high risk arm; - • not eligible for an immediate allogeneic HSCT or conventional chemotherapy - • all previous MDS specific therapies (except supportive approaches like transfusions or antibiotics) must have been discontinued at least 4 weeks prior to study enrollment; - • ECOG performance status of <= 3 at study entry (see Appendix 01); - • laboratory test results within these ranges:

- Serum creatinine <= 177 ìmo/l (<= 2.0 mg/dL);
- total bilirubin <= 3 x ULN;
- AST (SGOT) and ALT (SGPT) <= 3 x ULN;
- total fasting cholesterol <= 9.1 mmol/l (350 mg/dl);
- fasting triglyceride level <= 4.5 mmol/l (400 mg/dl);
- platelets > 25 Gpt/l without transfusion support in patients with LOW- and INT-1 Risk according to IPSS;
- • signed informed consent

Exclusion Criteria

- • For Patients with LOW- or INT1-Risk according to IPSS: Thrombocytopenia below 25 Gpt/l (INT2- and HIGH-IPSS patients may be included irrespective of platelet count);
- • known hypersensitivity to temsirolimus, sirolimus or any components of the infusion solution (dl-alpha-tocopherol, propylene glycol, anhydrous citric acid, polysorbate 80, polyethylene glycol 400, dehydrated alcohol);
- • known hypersensitivity to macrolid antibiotics (because of structural similarities between this class of antibiotics and study medication);
- • 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 study;
- • known positive for HIV or any other uncontrolled infection;
- • presence of any other malignancy being not in complete remission for at least 3 years (previous chemotherapy for other malignancies is not an exclusion criteria);
- • necessity of therapeutic anticoagulation (excluding low dose ASS);
- • participation in an other clinical trial within the last 4 weeks
- • pregnant or breast feeding females (lactating females must agree not to breast feed while on study);
- • females of childbearing potential (FCBP) except those fulfilling at least one of the following criteria:
- post-menopausal (12 months of natural amenorrhea or 6 months of amenorrhea with serum FSH > 40 U/ml);
- post-surgery (6 weeks after bilateral ovarectomy with or without hysterectomy);
- regular and correct use of contraceptives with a PEARL Index of < 1% (e.g. implants, depot formulations of hormones, oral contraceptives, intra uterine device – IUD);
- male patients, who do not agree to use a latex condom during sexual contact with females of childbearing potential while participating in the study and for at least 3 months following discontinuation from the study even if he has undergone a successful vasectomy;
- • patients with a history of chronic drug abuse or another illness which does not allow the patient to assess the nature and/or possible consquences of the study;
- • patients who are not likely to follow the trial protocol (lack of willingness to cooperate).

Age >= 18 years

Status Closed

start of Recruitment 15.12.2009

Recruiting countries Germany

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Other Registers	ClinicalTrials.govNCT01111448 (Primary Register) European Clinical Trials Database - EUDRACT2009-014768-21
Interventions	- • treatment with single agent Temsirolimus 25 mg/day on day 1; 8; 15; 22 of each 28-day cycle as intravenous infusion