Public Title	Phase I/II Trial in patientes > 60 years with AML with Azacitidine and Chemotherapy
Scientific Title	Response-Adapted Sequential Azacitidine And Chemotherapy in Patients > 60 Years Old With Newly Diagnosed AML Eligible for Chemotherapy and allogeneic hematopoietic cell transplantation: A Multicentre Phase I/II study of the East German Hematology and Oncology Study Group (OSHO)
Short Title	RAS-AZIC (OSHO #083)
Id KN/ELN	LN_OSHO_2012_558
Trialgoup	OSHO
Type of Trial	multicentric
Phase	Phase I/II
Disease	Acute myeloid leukemia(AML) AML all subtypes without FAB M3
Stage of Disease	de novo/non-treated - Therapy concepts for all genotypes - >= 60 years

Aim

- The objective of the trial is to assess efficacy and safety of induction therapy with response-adapted sequential azacitidine and conventional AML induction chemotherapy in patients > 60 years with newly diagnosed AML (at the dose level resulting from the dose evaluation phase of the trial).
- To assess efficacy in terms of the overall response rate (ORR) till day 90 including: - Complete remissions (CR) - Complete Remission with incomplete blood count recovery (CRi) - Partial remissions (PR)
- Safety of response-adapted sequential azacitidine and chemotherapy
- Overall survival one year after start of trial therapy
- Overall survival two years after start of trial therapy
- Event-free survival one and two years after start of trial therapy
- Days alive and out of hospital
- Rate of treatment failure according to IWG response criteria
- Number of patients undergoing HCT
- Correlate study endpoints with the points achieved at the time of diagnosis according to the following questionnaire: instrumental activities of daily living (iADLs, “Instrumentelle Aktivitäten des täglichen Lebens”)
- Correlate study endpoints with the Eastern Cooperative Oncology Group (ECOG) Performance Status at the time of diagnosis
- Compare response and survival in patients treated with response-adapted sequential azacitidine and chemotherapy with historical patient populations treated with the same conventional chemotherapy

Inclusion Criteria

- Subjects must meet ALL of the following criteria to be enrolled in the study: 1. Newly diagnosed (within the last 28 days) and untreated AML (> 20% blasts in the bone marrow based on the WHO classification) including: - de novo AML - AML secondary to prior myelodysplastic disease - AML secondary to exposure to potentially leukemogenic therapies or agents (eg, radiation therapy, alkylating agents, topoisomerase II inhibitors) with the primary malignancy in remission for at least 2 years
- 2. Age > 60 years
- 3. Eligible for intensive chemotherapy and allogeneic hematopoietic cell transplantation
- 4. Serum bilirubin levels <= 1.5 x the upper limit of normal (ULN). Higher levels are acceptable if these can be attributed to - active hemolysis (as indicated by positive direct Coombs’ testing, decreased haptoglobin level, elevated indirect bilirubin and/or lactate dehydrogenase [LDH]), - or ineffective erythropoiesis (as indicated by bone marrow findings)

	- 5. Serum glutamic-oxaloacetic transaminase (SGOT) (aspartate aminotransferase [AST]) level <= 2 x ULN - 6. Serum glutamic-pyruvic transaminase (SGPT) (alanine aminotransferase [ALT]) level <= 2 x ULN - 7. serum creatinine levels <= 1.5 x ULN - 8. Women of childbearing potential may participate, providing they meet the following conditions: - must agree to use effective contraceptive methods throughout the study and for 3 months following the date of the last dose of study medication - must have a negative serum pregnancy test obtained within 72 hours prior to day 1. - 9. Males with female partner of childbearing potential must agree to use effective contraceptive methods throughout the study and should avoid fathering a child for 3 months following the date of the last dose of study medication. - 10. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2 (Appendix A) 11. Capable of giving informed consent 12. Written informed consent
Exclusion Criteria	- 1. Acute promyelocytic leukaemia (AML M3) - 2. Previous cytotoxic or any other hypomethylating or biological treatment for AML, exception: hydroxyurea - 3. Any diagnosis of malignant disease within the previous 12 months (excluding basal cell carcinoma with no complications) - 4. Hepatic tumors in the medical history - 5. Known or suspected hypersensitivity to azacitidine or mannitol - 6. Patients with serious concomitant medical illness: - severe congestive heart failure [grade 3 according to CTCAE] or - clinically unstable ischemia or - acute myocardial infarction in the previous six months or - pulmonary hypertension [grade > 3 according to CTCAE] or - severe cardiac arrythmias [grade > 3 according to CTCAE] or - chronic pulmonary diseases [grade > 3 according to CTCAE] or - uncontrolled hypertension or - uncontrolled diabetes or - uncontrolled severe infections [grade > 3 according to CTCAE] or - any other severe or uncontrolled medical illness - 7. Psychiatric illness that would prevent granting of informed consent - 8. Active viral infection with known human immunodeficiency virus (HIV) or viral hepatitis type B or C - 9. Treatment with any of the following concomitant medications: - Corticosteroids, unless otherwise indicated, e.g. blood product transfusion reaction or prevention - Retinoids - Cytokines (except as outlined in Section 3.2.1) - Interleukin-11 - EPO - 10. Participation in other clinical trials in the last 30 days
Age	> 60 years
Status	No longer recruiting
start of Recruitment	31.08.2012
Recruiting countries	Germany
Target Sample Size	113
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