Public Title	Phase III Trial of Decitabine with or without Hydroxyurea versus Hydroxyurea in CMML
Scientific Title	A Randomized Phase III study of Decitabine with or without Hydroxyurea versus Hydroxyurea in patients with advanced proliferative Chronic Myelomonocytic Leukemia (GFM-DAC-CMML)
Short Title	DACOTA
Id KN/ELN	LN_DEUTSC_2014_566
Trialgoup	Deutsche MDS
Type of Trial	multicentric, randomized, double-group
Phase	Phase III
Disease	Myelodysplastic Syndrome(MDS) Different risk groups
Stage of Disease	.
Aim	- To compare between both arms the event-free survival (EFS).
Inclusion Criteria	- 1. Age 18 and older - 2. CMML as defined by: - Diagnosis according to WHO criteria - Stable excess in blood monocytes, > 1 Giga/L - Lack of bcr-abl rearrangement (or Philadelphia chromosome) - Bone marrow blast cells < 20% - Dysplasia of at least one lineage or clonality marker or blood monocytosis during more than 3 months w/o other explanation. - And WBC >= 13 G/L - And - At least two of the following criteria: (adapted from Wattel et al. Blood 1996) - Marrow blasts >= 5 % - Clonal cytogenetic abnormality other than t(5;12) (q33; p13) and loss of Y chromosome - ANC > 16 G/l in the absence of an active infection - Anemia (Hb < 10 g/dL) - Thrombocytopenia (platelet count < 100 G/L) - Splenomegaly > 5 cm below costal margin (spleen size should also be measured by an imaging technique) - Or: Extramedullary localization (including documented cutaneous, pleural or pericardial effusion) - 3. No prior treatment (except supportive care, or ESA, or short term (< 6 weeks) HY in patients presenting with high WBC counts) - 4. Performance status 0-2 on the Eastern Cooperative Oncology Group (ECOG) Scale. - 5. Adequate organ function including the following - Liver: total bilirubin < 1.5 times upper limit of normal (ULN) (except moderate unconjugated hyperbilirubinemia due to intra medullary hemolysis or due to Gilbert syndrome) , alanine transaminase (ALT) and aspartate transaminase (AST) < 3 times ULN - Renal: serum creatinine < 2 times ULN - 6. Signed informed consent - 7. Negative pregnancy and adequate contraception (including in male patients) if relevant. Female subjects of chilbearing potential must:

- Agree to have a medically supervised pregnancy test on the day of the study visit or in the 3 days prior to the study visit once the subject has been on effective contraception for at least 4 weeks. This requirement also applies to women of childbearing potential who practice complete and continued abstinence. The test should ensure the subject is not pregnant when she starts treatment.
- Agree to have a medically supervised pregnancy test every 4 weeks including 4 weeks after the end of study treatment, except in the case of confirmed tubal sterilization. These pregnancy tests should be performed on the day of the study visit or in the 3 days prior to the study visit. This requirement also applies to women of childbearing potential who practice complete and continued abstinence.
- Agree to use, and to be able to comply with, effective contraception without interruption, 4 weeks before starting study drug throughout the entire duration study drug therapy (including doses interruptions) and for 3 months after the end of the study drug therapy even if she has amenorrhoea. This applies unless the subject commits to absolute and continuous abstinence confirmed on a monthly basis, to avoid pregnancy for the duration of study.
- The following can be considered to be examples of suitable methods of contraception for female patients: implant, levonorgestrel-releasing intrauterine system (IUS), medroxyprogesterone acetate depot, tubal sterilisation, sexual intercourse with a vasectomised male partner only (vasectomy must be confirmed by two negative semen analyses), ovulation inhibitory progesterone-only pills (i.e., desogestrel). If not established on effective contraception, the female subject must be referred to an appropriately trained health care professional for contraceptive advice in order that contraception can be initiated.
- Implants and levonorgestrel-releasing intrauterine systems are associated with an increased risk of infection at the time of insertion and irregular vaginal bleeding. Prophylactic antibiotics should be considered particularly in patients with neutropenia
- Copper-releasing intrauterine devices are generally not recommended due to the potential risks of infection at the time of insertion and menstrual blood loss which may compromise patients with neutropenia or thrombocytopenia.
- - Understand that even if she has amenorrhea, she must follow all the advice on effective contraception - She understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy
- Male patients must : - Agree the use of a condom if engaged in sexual activity with a pregnant woman or a woman of childbearing potential, during the entire period of treatment, even if dysruption of treatment and during 3 months after end of treatment

Exclusion Criteria

- Myeloproliferative / myelodysplastic syndrome other than CMML
- Patients eligible for allogeneic bone marrow transplantation with an identified donor
- CMML with t(5;12) or PDGFßR rearrangement that may be treated with imatinib
- Pregnant or breastfeeding
- Performance status > 2 on the ECOG Scale.
- Serious concomitant systemic disorder, including active bacterial, fungal or viral infection that in the opinion of the investigator, would compromise the safety of the patient and/or his/her ability to complete the stud
- Prior malignancy (except in situ cervix carcinoma, limited basal cell carcinoma, or other tumors if not active during the last 3 years)

Age	>= 18 years
Status	Active
start of Recruitment	31.10.2014
Recruiting countries	Germany
	France

	Italy
Target Sample Size	168
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Centre of Trial	Universitätsklinikum Carl Gustav Carus, Dresden
Sponsors	Gesellschaft fur Medizinische Innovation – Hamatologie und Onkologie mbH
Supporters	Janssen-Cilag International NV
Other Registers	European Clinical Trials Database - EUDRACT2014-000200-10
Therapy	Decitabine (DAC) with or without Hydroxyurea (HY) versus HY only. Concomitant treatments: Best Supportive Care: Transfusion, other supportive care as needed (excluding growth factors). Hydroxyurea will be allowed in the decitabine arm during the first three cycles if WBC counts > 30 G/L and mandatory if WBC > 50 G/L.