SAMENVATTING Hovon 155 AML

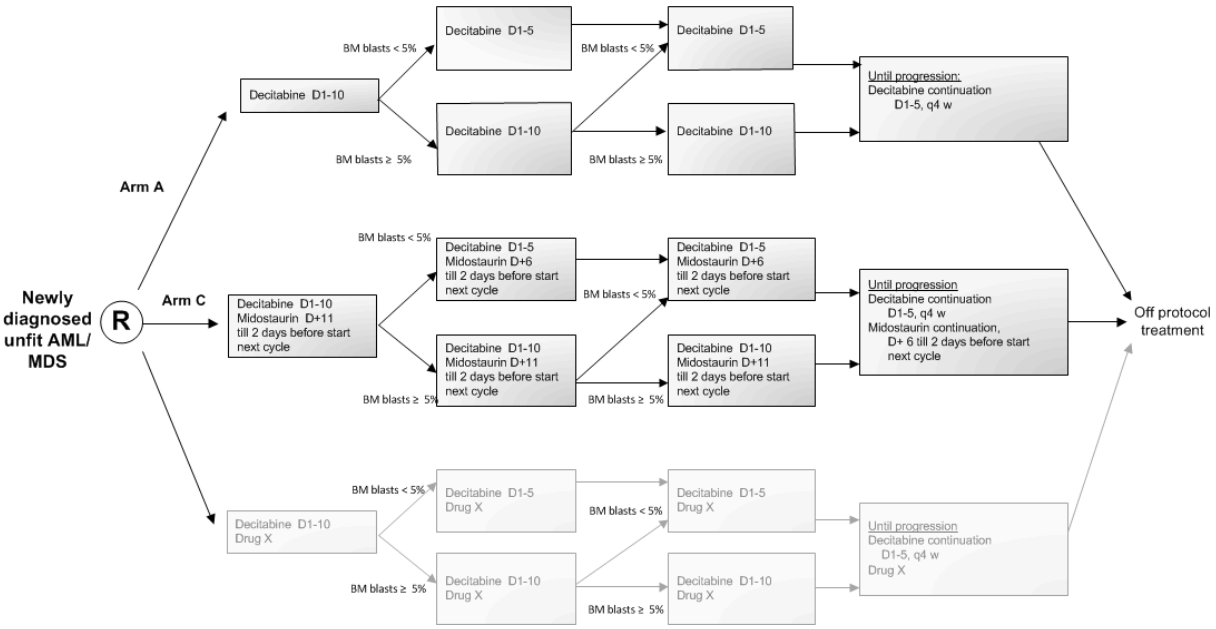
TITEL

A randomized phase II multicenter study to assess the tolerability and efficacy of the addition of midostaurin to 10-day decitabine in unfit (i.e. HCT-CI ≥ 3) adult AML and high risk myelodysplasia (MDS) (IPSS-R > 4.5) patients.

INDICATIE

Patients with AML (except APL) or high risk MDS (IPSS-R > 4.5), previously untreated, age ≥ 18 yrs AND Hematopoietic Cell Transplantation Co-morbidity Index (HCT-CI) ≥ 3 OR who do not want intensive chemotherapy (wish of the patient).

SCHEMA



INCLUSIE CRITERIA

1. Patients with:
   - a diagnosis of AML and related precursor neoplasms according to WHO 2016 classification (excluding acute promyelocytic leukemia) including secondary AML (after an antecedent hematological disease (e.g. MDS) and therapy-related AML, or
   - a diagnosis of myelodysplastic syndrome with excess of blasts (MDS) and IPSS-R > 4.5
2. Patients 18 years and older.
3. Patients NOT eligible for standard chemotherapy, defined as HCT-CI ≥ 3. (Appendix G) or Patients NOT eligible for standard chemotherapy for other reasons (wish of patient).
4. WBC ≤ 30 x10^9/L (prior hydroxyurea allowed for a maximum of 5 days, stop 2 days before start decitabine treatment)
5. Adequate renal and hepatic functions unless clearly disease related as indicated by the following laboratory values:

- Serum creatinine ≤ 221.7 µ mol/L (≤ 2.5 mg/dL), unless considered AML-related
- Serum bilirubin ≤ 2.5 x upper limit of normal (ULN), unless considered AML-related or due to Gilbert's syndrome
- Alanine transaminase (ALT) ≤ 2.5 x ULN, unless considered AML-related

6. WHO performance status 0, 1 or 2 (see Appendix D).
7. Patient is willing and able to use adequate contraception during and until 5 months after the last protocol treatment.
8. Written informed consent.
9. Patient is capable of giving informed consent.

EXCLUSIE CRITERIA

1. Acute promyelocytic leukemia.
2. Acute leukemia's of ambiguous lineage according to WHO 2016
3. Patient has symptomatic central nervous system (CNS) leukemia (NO routinely lumbar puncture required to investigate CNS involvement)
4. Blast crisis of chronic myeloid leukemia.
5. Diagnosis of any previous or concomitant malignancy is an exclusion criterion:
   - **except** when the patient completed successfully treatment (chemotherapy and/or surgery and/or radiotherapy) with curative intent for this malignancy at least 6 months prior to randomization. OR
   - **except** for basal and squamous cell carcinoma of the skin or in situ carcinoma of the cervix
6. Patients previously treated for AML (any antileukemic therapy including investigational agents), a short treatment period (≤ 5 days) with Hydroxyurea is allowed
7. Current concomitant chemotherapy, radiation therapy, or immunotherapy; other than hydroxyurea
8. Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, pulmonary disease etc.)
9. Cardiac dysfunction as defined by:
   - Myocardial infarction within the last 3 months of study entry, or
   - Reduced left ventricular function with an ejection fraction < 40% as measured by MUGA scan or echocardiogram or
   - Unstable angina or
   - New York Heart Association (NYHA) grade IV congestive heart failure (see Appendix I) or
   - Unstable cardiac arrhythmias.
10. History of stroke or intracranial hemorrhage within 6 months prior to randomization.
11. Patient has a history of human immunodeficiency virus (HIV) or active infection with Hepatitis C or B.
12. Patients known to be pregnant
13. Patients with a history of non-compliance to medical regimens or who are considered unreliable with respect to compliance.
14. Patients with any serious concomitant medical condition which could, in the opinion of the investigator, compromise participation in the study.
15. Patients who have senile dementia, mental impairment or any other psychiatric disorder that prohibits the patient from understanding and giving informed consent.
16. Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule