Decitabine in combination with chidamide, cytarabine and homoharringtonine(DCHA) as postremission therapy for acute myeloid leukemia with t(8;21) :A multicenter prospective study

Sponsor: Chinese PLA General Hospital

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Purpose

Acute myelocytic leukemia (AML) is a highly heterogeneous group of malignant hematopathy. Chromosomal translocation with t (8; 21) (q22; q22) , about 10 ~ 15% incidence in AML and 40% incidence in the AML-M2 type of leukemia, is a karyotype that is considered to have a good prognosis. The NCCN guidelines recommend that high-dose Ara-c regimens may benefit for patients, but with 30 to 40% relapse and serious risks on myelosuppression, infection and bleeding in high-dose Ara-c consolidation chemotherapy and more than 70% recurrence rate with KIT mutation. So the exploration of a relatively safe and efficient consolidation therapy is one of the difficult problems to be solved in the treatment of mitigatory t (8; 21) AML. We will investigate the safety and efficacy of a combination regimen including decitabine, chidamide, cytarabine and homoharringtonine as the postremission therapy for AML with t(8;21).

Primary Outcome Measure:

Progression free survival [Time Frame: 2 years]

Secondary Outcome Measures:

Overall survival [Time Frame: 2 years]

Estimated Enrollment: 120

Study Start Date: January 1, 2017

Estimated Study Completion Date: December 31, 2019

Estimated Primary Completion Date: December 31, 2018

Eligibility

Ages Eligible for Study: 14 Years to 65 Years

Sexes Eligible for Study: All

Gender Based: No

Inclusion Criteria:

Written informed consent provided.

The patients were diagnosed AML-M2 with t(8;21)(q22;q22) chromosomal changes and positive AML1-ETO fusion gene according to the 2008 World Health Organization (WHO) diagnostic criteria for malignant myeloid diseases.

Males or females aged ≥18 years, < 65 years.

ECOG performance status 0-3.

Life expectancy ≥3 months.

The morphology was Complete remission (CR) or Cri after 2 cycles of anthracycline induced chemotherapy.

No serious disease with heart, lung, liver and kidney.

The ability to understand and be willing to sign the Informed Consent Form of the experiment.

Patient who can start the investigational therapy within 3−6 weeks after the complete resection

Adequate liver function: Total bilirubin ≤ 1.5 x upper limit of normal (ULN), Aspartate aminotransferase (AST), alanine aminotransferase (ALT) ≤ 2.5 x ULN in subjects without liver metastases; ≤ 5 x ULN in subjects with liver metastases.

Adequate renal function: Serum creatinine ≤ 1.25 x ULN, or ≥ 60 ml/min.

Female subjects should not be pregnant or breast−feeding.

Exclusion Criteria:

Known allergic to prior treatment with drugs contained by the trial programme or with a chemical structure similar medicine.

Pregnancy, breast−feeding women and childbearing age patients who do not want to take contraceptive measures.

Active serious infection.

Patients with extramedullary lesions.

Patients who use drugs or drink alcohol for a long time to influence the evaluation of results.

Patients with mental illness or other conditions are unable to obtain knowledge and consent, and can not cooperate with the requirements of the completion of the test treatment and examination steps.

Patients with a history of the clinical significance of QTc prolongation (male > 450ms, female >470ms), ventricular tachycardia (VT), atrial fibrillation (AF), degree of heart block, muscle infarction (MI) within 1 years, congestive heart failure (CHF), with symptoms and drug therapy in patients with coronary heart disease.

Patients with abnormal liver function (total bilirubin > 1.5 x ULN, ALT/AST > 2.5 x ULN, or liver invasion ALT/AST > 5x ULN), renal function abnormality (serum creatinine > 1.5 x ULN).

The researchers decided that patient was not appropriate to take part in the experiment.

Treatment regimen

HA:

homoharringtonine 2mg IV d1-5

cytarabine(Ara-C) 1500mg/m^2(<60 year old) ; 1000mg/m^2(>60 year old)

IV q12h d1,3,5

DCHA:

Decitabine 20mg/m^2 d8-12

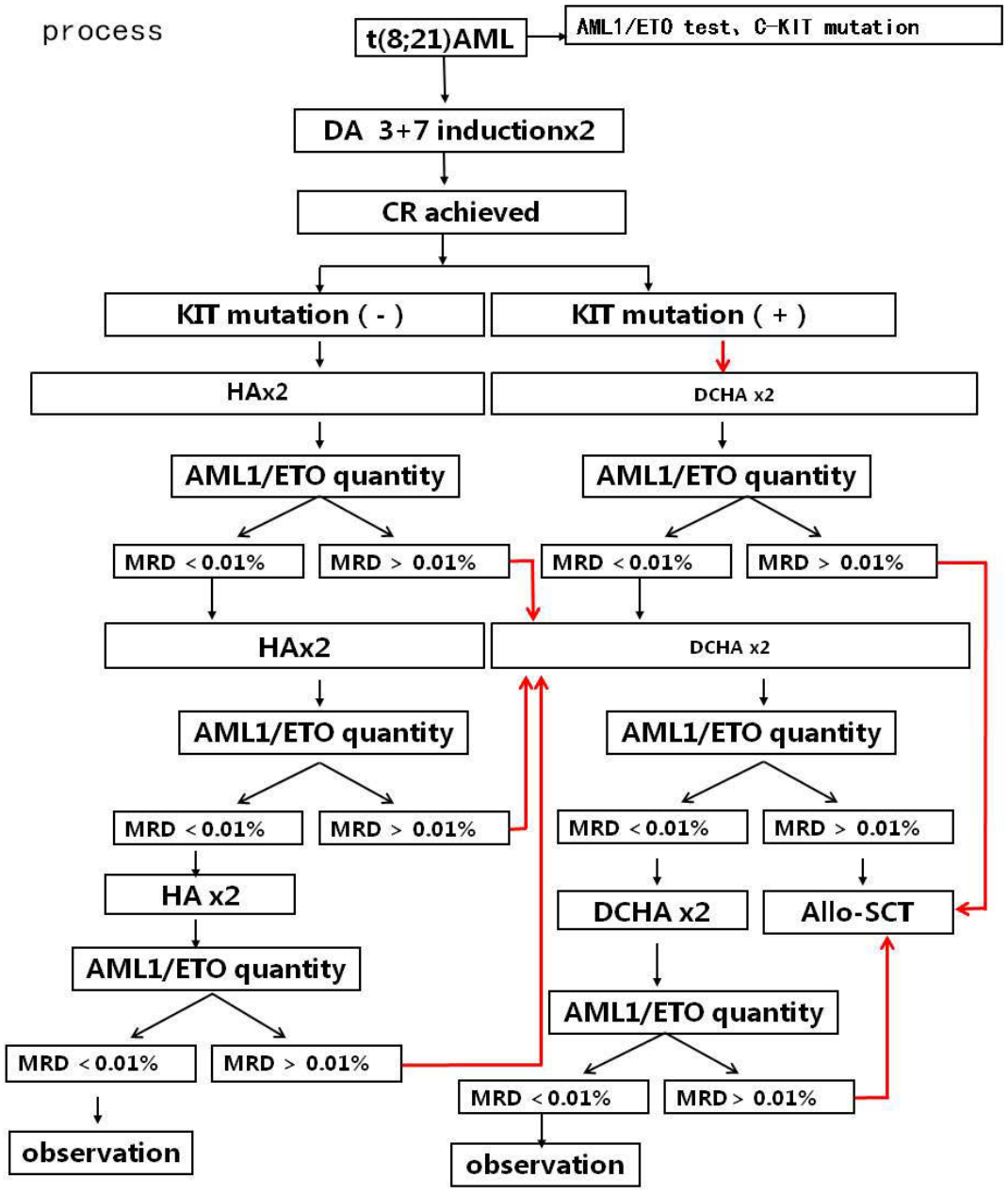
Chidamide 30mg twice/week P.O. for two weeks per cycle (four doses totally)

cytarabine(Ara-C) 1500mg/m^2(<60 year old) ; 1000mg/m^2(>60 year old)

IV q12h d1,3,5

homoharringtonine 2mg IV d10-14

Process schedule



Statistical analysis

SAS 9.0 software (SAS Institute) will be used in all statistical

analysis. Survival data were analyzed by the log-rank test, and survival curves will be plotted with the Kaplan-Meier method. *t* test will be used to assess the probability of significant differences of survival time. $P < 0.05$ was considered statistically significant.