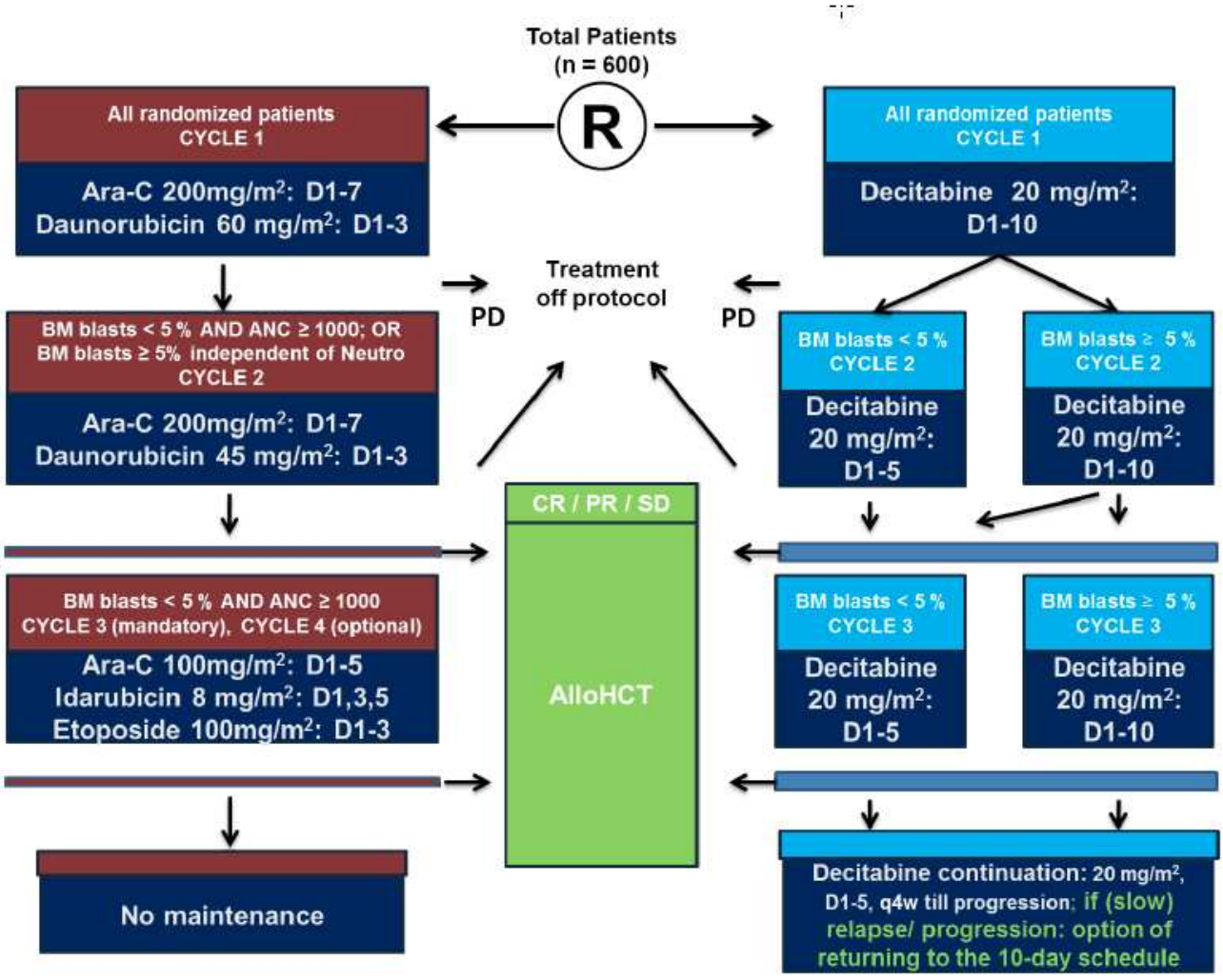
SAMENVATTING EORTC-1301-LG

TITEL

10-day decitabine versus conventional chemotherapy ("3+7") followed by allografting in AML patients ≥ 60 years: a randomized phase III study of the EORTC Leukemia Group, CELG, GIMEMA and German MDS Study Group.

INDICATIE

Acute Myeloid Leukemia (AML) ≥ 60 Years old, fit to receive intensive treatment



Cytarabine (Ara-C); bone marrow (BM); absolute neutrophil count (ANC); progressive disease (PD); complete remission (CR); partial remission (PR); stable disease (SD); allogeneic hematopoietic stem cell transplantation (alloHCT).

INCLUSIECRITERIA

Patients are eligible for the study if:

♦ Age ≥ 60 years

♦ WHO Performance status: ≤ 2 (Appendix C)

♦ Eligible for standard intensive chemotherapy

♦ Have newly diagnosed AML that is cytopathologically confirmed according to the WHO classification (Appendix K) (Patients can be diagnosed with AML two months prior to randomization)

♦ Absence of acute promyelocytic leukemia (APL), i.e. AML-M3 with t(15;17)(q22;q12); PML-RARA fusion gene and cytogenetic variants)

♦ De novo or secondary AML is allowed [Of note: secondary AML includes AML developed following cytotoxic/genotoxic exposure or AML developed following a history of malignant or non-malignant disease]

♦ Absence of blast crisis of chronic myeloid leukemia

♦ Absence of active central nervous system (CNS) leukemia

♦ WBC is ≤30x10^9/L (measured within 72 hours prior to randomization) [Of note: HU treatment is allowed to reach this eligibility criterion]

♦ The following laboratory assessments should be done within 7 days prior to randomization and should be within the following range:

♦ SGOT (ASAT) and SGPT (ALAT) < 2.5 x the upper limit of normal range (at the laboratory where the analyses were performed) unless considered AML-related

♦ Total serum bilirubin level < 2.5 x the upper limit of normal range (at the laboratory where the analyses were performed) unless considered AML-related or due to Gilbert's syndrome

♦ Serum creatinine concentration < 2.5 x the upper limit of normal range (at the laboratory where the analyses were performed) unless considered AML-related

♦ Patients did not receive any prior treatment **for AML** (relapsed AML is not allowed), such as any antileukemic therapy including investigational agents and hypomethylating agents (decitabine, 5-azacytidine). Treatment with HU is allowed to control the leukocytosis if given for a maximum of 5 days

♦ Patients did not receive prior treatment for **MDS or MPN** with:

♦ hypomethylating agents (decitabine, 5-azacytidine), OR

♦ with intensive chemotherapy or transplantation within the last three years

♦ NOTE: The following treatments for previous **MDS or MPN** are allowed as long as treatment has stopped at least one month before inclusion:

♦ Growth factors, thrombomimetics, immunosuppression (cyclosporine A, steroids, Antithymocyte globulin etc.), chelation, interferons, anagrelide

♦ Lenalidomide, low-dose chemotherapy (low-dose melphalan, HU, low-dose cytarabine etc.), tyrosine-kinase inhibitors, histone deacetylase inhibitors (e.g. valproic acid, panobinostat etc.), mTOR inhibitors, other experimental treatment that is not based on inhibition of DNA methyltransferase

♦ Absence of concomitant severe cardiovascular disease which would make intensive chemotherapy impossible, i.e. arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease, reduced left ventricular function assessed by multigated acquisition (MUGA) scan or echocardiogram

♦ Absence of concomitant malignancy or any malignancy requiring chemotherapy (except basal and squamous cell carcinoma of the skin) for which the patient received chemotherapy within 6 months prior to randomization

Note: diagnosis of any previous or concomitant malignancy is thus not an exclusion criterion.

♦ Absence of active uncontrolled infection

♦ Patients of reproductive potential should use adequate birth control measures, as defined by the investigator, during the study treatment period and for at least 3 months after the last study treatment. A highly effective method of birth control is defined as those which result in low failure rate (i.e. less than 1% per year) when used consistently and correctly

♦ Absence of any psychological, familial, sociological or geographical condition, in the opinion of the investigator, potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before randomization in the trial

♦ Before patient registration/randomization, written informed consent must be given according to the International Conference on Harmonisation good clinical practice (ICH GCP) and national/local regulations

Important note: All eligibility criteria must be adhered to.