GENETIC RANDOMIZATION AS A PREREQUISITE FOR SURVIVAL COMPARISON BETWEEN ALLOGENEIC STEM CELL TRANSPLANTATION AND CONSERVATIVE DRUG TREATMENT

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Treatment options for patients with chronic myeloid leukemia (CML) are early allogeneic stem cell transplantation (SCT) or conservative drug treatment. The comparison of survival between SCT and drug treatment held two statistical main problems: a) the selection of patients for SCT was uncontrolled and not at random, b) the time from diagnosis to SCT had to be considered in an unbiased manner. Comparing survival by the Mantel-Byar test can overcome "time-to-transplantation" but not selection bias. Entering the German CML-study III, patients were checked for "eligibility for and consent to SCT". Upon qualification and agreement, the availability of a related donor was instantly investigated. Patients with a related donor were assigned to "early SCT", all others to "conservative drug treatment". Availability of a related donor could be regarded as a random criterion without influence on survival time. By considering survival from diagnosis also for the SCT arm, patients were at risk while receiving conditioning therapy and waiting for transplantation. Conversely, survival times up to the day of transplantation contributed in favor of the SCT arm. Following "intention-to-treat", the two treatment strategies could be appropriately considered in an unbiased manner. The study design proved to be feasible, 123 of 135 patients allocated to SCT were actually transplanted, 6 died before. Logistic functions related, survival between the two arms was compared by the Wilcoxon-Gehan test.