

Clinical trials for MDS by Japan Adult Leukemia Study Group

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Japan Adult Leukemia Study Group (JALSG) is a study group for adult leukemia and related diseases including MDS in Japan, and has been conducting many clinical trials. In the JALSG-MDS200 trial, we tried to evaluate the efficacy of dose-adjusted intensive induction chemotherapy (DA-IC) for higher risk MDS. Patients were randomly assigned to DA-IC or low dose chemotherapy (low dose AraC and aclarubicin, LDCA), comparing CR rate and survival. Although CR rate was higher in DA-IC, there was no difference in survival between the DA-IC and LDCA groups, suggesting the limitation of classical chemotherapeutic agents for higher risk MDS. After the emergence of azacytidine (AZA) for MDS treatment, we conducted a randomized trial comparing 7-day AZA administration (AZA-7) and 5-day regimen (AZA-5) for higher risk MDS (JALSG-MDS212 study). Unfortunately, this study was terminated prematurely because of slow recruitment. In the protocol defined interim analysis, there was more than 10% difference in 2-year survival rate (36.4% in AZA-7, and 25.8% in AZA-5, respectively, $P=0.293$), and the number of leukemia transformation was higher in AZA-5 (40 out of 92 patients in AZA-7, and 54 out of 95 patients in AZA-5, respectively). Although we did not observe statistically significant difference in time to leukemia transformation between AZA-7 and AZA-5 in all patients, the analyses using centrally reviewed cases demonstrated that AZA-7 had significantly longer time to leukemia transformation than AZA-5. Clinical samples collected during JALSG-MDS212 study and samples from other groups were analyzed together for the molecular efficacy of AZA, and we found that the clone size after AZA treatment has a significant impact on clinical results.