Anthracycline dose intensification improves molecular response and outcome of patients treated for core binding factor acute myeloid leukemia

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MRD levels were serially monitored for *RUNX1-RUNX1T1* or *CBFB-MYH11* transcripts by real-time quantitative polymerase chain reaction in 3 laboratories (Marseille, Angers, Toulouse), as described previously (1). CBF transcript level was assessed on blood or marrow before induction (baseline), after induction (MRD1), cycle 1 (MRD2), and cycle 2 (MRD3) of consolidation. For each individual patient, only one type of sample (i.e. blood or marrow) was considered. Major molecular response was defined as a 1000 fold reduction (3 log) of normalized CBF transcript compared to diagnosis level. Complete molecular response was defined as an undetectable transcript with a detection threshold of at least 10^{-4} copies.

Statistics

Data were summarized by frequency and percentage for categorical variables. For continuous variables, the median and range were computed. Statistical tests were two-sided at the 5% level of significance. Univariate analyses were performed using non parametric Wilcoxon rank sum test or Kruskal-Wallis rank sum test when appropriate. Survival rates were estimated by the Kaplan-Meier method. Overall survival (OS) was defined by the time interval from the date of the induction chemotherapy until death from any cause with observation ending at the date of last contact for patients last known to be alive. Relapse Free survival (RFS) was defined by the time interval from the date of the remission until death from any cause or relapses with observation ending at the date of last contact for patients last known to be alive.. Patients without event were censored at the date of the last follow up or at date of allogeneic transplantation (if transplantation was performed in first CR). Multivariate analyses were performed using a Cox method or logistic regression method when appropriate. All variable with p-value below 0.15 in univariate analysis were included in the Cox model using a stepwise procedure selection. Statistical analysis was performed using the SPSS 16.0 software.

1. Gabert J, Beillard E, van der Velden VH, Bi W, Grimwade D, Pallisgaard N, et al. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program. Leukemia. 2003 Dec;17(12):2318-57.

Supplemental table 1

	Overall survival			Relapse free survival		
Variable	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
CBF subtype t(8;21) vs. Inv(16)	0.25	[0.37-0.81]	0.03	0.25 0.25	[0.11-0.86] [0.08-0.72]	0.03 0.01*
Schedule DNR90 vs. DNR60	0.18	[0.03-1.4]	0.12	0.2 0.15	[0.03-0.51] [0.04-0.65]	0.006 0.01*
Platelet at diagnosis continuous	0.98	[0.96-0.99]	0.03	1.0	[0.996-1.01]	0.44
MMR1* MMR1 vs no MMR1				0.42*	[0.18-1]*	0.051*

Supplemental table 1. Multivariate analysis of outcome

OR: Odd Ratio, 95% CI: 95% Confidence interval. A Cox model was used for all of these analyses

*: MMR1 was integrated in a separated MVA model for PFS, results with * shows the OR, 95%CI and p values with this model