

ACUTE LEUKEMIAS

## WT1 REDUCTION AFTER INDUCTION THERAPY PREDICTS OUTCOME IN AML PATIENTS

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**Background:** WT1 gene is overexpressed in 75-80% of adult Acute Myeloid Leukemia (AML) patients, and its expression is associated with different molecular alterations such as FLT3-ITD, NPM1 mutation, inv (16). Its overexpression would make it an optimal candidate as a marker in the prognostic evaluation at diagnosis and in the evaluation of minimal residual disease (MRD). However, the clinical and prognostic significance of WT1 expression in AML patients is still controversial and not fully investigated.

**Aims and Methods:** This is a retrospective study with the aim of evaluating the possible role of the WT1 value as prognostic marker at diagnosis and in the evaluation of MRD in a cohort of AML patients referring to the Hematology Units of Siena and Ravenna from 2008 to 2025.

**Results:** 120 AML patients overexpressing WT1 have been studied: 61 male and 59 female, with a median age at diagnosis of 59 years [IQR 49-66,5]. Among these, 44 (36,7%) were high-risk AML, 50 (41,7%) were intermediate-risk AML, and 26 (21,6%) were low-risk AML. The median WT1 value at diagnosis was 4559 [IQR 2248,42, 9607,75] while after the induction therapy was 122 copies [IQR 41,50, 622,50]. Comparing WT1 values at diagnosis with white blood cell count and

blast count, a correlation was documented ( $\rho=0.46$  and  $\rho=0.314$  respectively, by Spearman' test) while there was no statistically significant correlation with LDH and with main genetic mutations (NPM1 and FLT3). Regarding the role of WT1 in assessing MRD, WT1 values were monitored following induction chemotherapy. Considering WT1 value at diagnosis and post-induction, a reduction greater than two logarithms correlated with the Overall survival (OS) and Event Free Survival (EFS) ( $p=0.0024$  and  $p=0.0091$ , respectively) (Figure 1), particularly in presence of NPM1 mutation ( $p=0.013$ ) (Figure 2). On the contrary, the presence of FLT3 mutation and a WT1 reduction  $< 2\log$ , correlated with a worse OS (Figure 2).

**Conclusions:** In conclusion, despite the limitations of a small sample size, our study documented a potential role for WT1 as a marker of MRD, as the greater than two-log reduction after induction chemotherapy correlates with OS and EFS, offering an alternative opportunity to monitor MRD in AML patients. For this reason, it could be useful to value WT1 expression in AML patients at diagnosis and after chemotherapy, especially with lacking molecular or immunophenotypic markers, in order to better explore the potential of WT1 as an MRD marker in this patient setting.

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Figure 1. OS and EFS

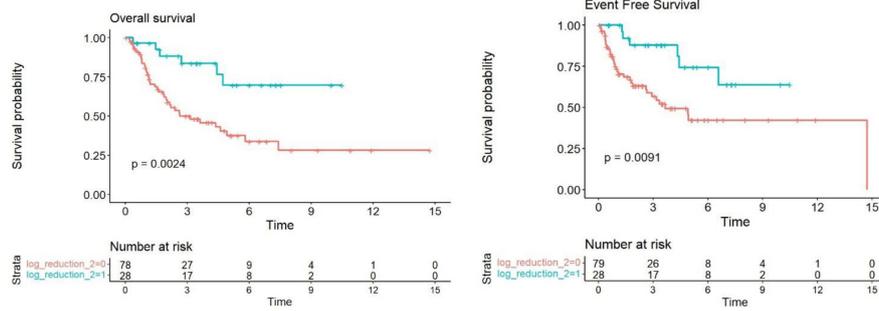


Figure 2. OS according to presence/absence of NPM1 and FLT3 mutations.

