What should be the Therapy for CD25 Positive Acute Myelogenous Leukemia?

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Editorial

A recent analysis of the Eastern Cooperative Oncology Group E1900 study by Gönen et al. [1] showed that the presence of CD25 at diagnosis identifies AML patients with shorter relapse free survival (RFS) as well as overall survival (OS). A smaller group of AML patients previously analyzed by the HOVON group showed that CD25 expression is associated with shortened RFS and OS [2]. Both studies compared induction chemotherapy with standard versus escalated anthracycline dose followed by Stem Cell Transplantation (SCT) or high dose cytarabine (HiDAC). Gönen et al. also described our recent related analysis [3]. We have performed additional analyses of our cohort and would like to highlight differences from the two aforementioned studies [4].

We further analyzed patients by flow cytometry and found that 16% of initially CD25 negative patients became CD25 positive at the time of relapse. Among CD25 positive patients who experienced progression or relapse, 21% showed a higher percentage of CD25 positive cells at progression/relapse than at initial diagnosis [3]. It would be valuable to know the frequency of these phenomena in a large study such as E1900. We did not observe a difference in OS between CD25 positive versus CD25 negative patients (Table 1), but we noted a markedly increased cumulative incidence of relapse in CD25 positive patients (p=0.0012, Table 1). Many CD25 positive patients also carried Flt3-ITD mutation which, in preclinical models, confers sensitivity to cytarabine, but anthracyclines do not seem to add much activity [5].

Table 1: Overall survival (OS), relapse free survival (RFS), complete response (CR), not available (n.a.), autologous stem cell transplantation (ASCT), cumulative incidence of relapse (CIR), patients (pts), high dose cytarabine (HiDAC), not significant (ns). The induction regimen in our study was HiDAC and anthracycline (mitoxantrone) [6] and we utilized a modification of the HiDAC regimen described by Herzig et al. [7] as salvage chemotherapy. Escalated anthracycline dosing did not change the poor outcome of CD25 positive AML [1,2] but we found that patients who receive therapy containing high-dose cytarabine may be salvaged. Finally, we observed that hematopoietic SCT (allogeneic more than autologous) appeared to have a positive impact on patient survival [3,4].

In summary, we recommend that high-dose cytarabine and allogeneic stem cell transplantation should be considered when treating patient with CD25 positive AML. Continued prospective analysis of this high-risk subset of AML needs to be completed, while incorporation of rationale targeted agents should be integrated into the therapeutic paradigm.
References


