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Editorial Open Access

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].

	CD25 negative	CD25 positive
HOVON 42,HOVON 42a and HOVON432	65 evaluable pts; treatments:	
	All protocols had an identical design, consisting of at least two cycles of remission induction therapy with standard dose cytarabine and anthracycline. Patients in CR after two cycles of Chemotherapy received either allogenic or autologous stem cell transplantation or received a third course of intensive chemotherapy.	
Median OS (months), p= 0.00045	> 48	10
Median RFS (months), p= 0.005	> 47	7
ECOG 19001	396 pts with detailed mutational analysis; 3 daily doses of daunorubicin at either the standard dose (45 mg/m2) or a high dose (90 mg/m2), combined with 7 daily doses of cytarabine (100 mg/m2) by continuous	
	intravenous infusion. Patients in CR were offered either allogeneic SCT or HiDAC +/- a single dose of the monoclonal antibody gemtuzumab ozogamicin, followed by autologous SCT.	
Median OS (months) with SCT, p=0.001	Not reached (at 54 months)	10.8
Median RFS (months)	n.a.	n.a.
UMASS4	45 evaluable pts; (HiDAC) and high dose	
	mitoxantrone (cytarabine at dose 3 g/m2 daily on days 1-5; mitoxantrone 80 mg/m2 on day 2), or HiDAC with duanorubicin (cytarabine 3 g/m^2 given for total of eight doses followed by daunorubicin 60 mg/m2 daily for 2 days)	
Median OS (months), p=ns	Not reached	Not reached (at 54 months)
Median CIR (months), p=0.0012	Not reached	2.3

Table1: 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 anthacendione (mitoxanthrone) [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.

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