

ROLE OF ALLOGRAFTING IN ACUTE LYMPHOBLASTIC LEUKEMIA: A 12 YEAR EXPERIENCE

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Background. Acute lymphoblastic leukemia (ALL) is a rare disease in adults. Despite the introduction of several novelties in this field in terms of prognostic factors and new therapies, clinical outcomes remain unsatisfactory.

Aim of the study. To evaluate the experience on 84 consecutive patients diagnosed with ALL at the Divisions of Hematology, S. Giovanni Battista Hospital, Torino, between 1999-2011.

Methods. Patients, median age 49 years (18-73), were treated according to Center guidelines or on clinical trials active at the time of diagnosis. At diagnosis, patients who presented with leukocytosis, poor-prognosis cytogenetic abnormalities, or delayed response to induction therapy were defined as high risk. High risk patients younger than 60 were considered for allografting (SCT) as part of first-line treatment. Treatments for 80% (20/25) of patients with traslocation (9;22) also included tyrosine kinase inhibitors after 2002: in 14 as part of induction, in 4 as maintenance and in 2 as salvage treatment..

Results. Overall, 25% (21/84) presented with leukocytosis and 56% (38/68, not done in 16) had poor-prognosis cytogenetic abnormalities. Complete remission (CR) was achieved in 92% of patients (77/84). After a median follow-up of 5 years (3-143 months), 43% of patients are alive, with a median overall survival (OS) and event-free survival (EFS) of 2 and 1,6 years, respectively. Forty patients received an allograft in first (no.=32) or second (no.=7) complete remission, or in progression (no.=1), from a HLA identical sibling (no.=21), an unrelated (no.=17) or a related other than sibling (no.=2) donor. Cumulative incidences of acute and chronic graft-versus-host disease were 47% and 39%, respectively. Median OS and EFS in patients who received SCT were 60 months and not reached, respectively, whereas in those younger than 60 who did not undergo a SCT median OS and EFS were 16 and 13 months (p=0.024 and 0.026) respectively. Stratifying patients by year of diagnosis, a trend toward improved EFS in those diagnosed after 2008 as compared to those diagnosed before 2003 (2.3 years versus 1.3) was observed, whereas OS remained super-imposable. By multivariate analysis, the prognostic role of leukocytosis at diagnosis was confirmed for both OS and EFS (HR 2.48, IC 95% 1.28-4.80, p=0.007, and HR 3.72, IC 95% 1.93-7.14, p<0.001, respectively). Furthermore, in younger patients, an advantage in those who received an allograft in terms of both OS (HR 0.11 CI 95% 0.03-0.44 p=0.002) and EFS (HR 0.12 CI 95% 0.03-0.47 p=0.002) was seen.

Conclusions. SCT played a significant role in improving survival in patients with ALL, though prognosis in patients with leukocytosis or older remained poor. The trend toward an improved outcome seen in more recent years may be due to less toxic transplant procedures and the introduction of "minimal residual disease-guided treatment" and the availability of tyrosin kinase inhibitors. The combination of allografting and tyrosin kinase inhibitors, or novel monoclonal antibodies such as blinatumomab, should be evaluated in prospective control trials.

Keywords: acute lymphoblastic leukemia, allogeneic stem cell transplant (o allografting), leukocytoses

Topic: acute lymphoid leukemia, clinical