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Survival Improvement Of Secondary Acute Myeloid Leukemia Over Time: Experience From 962 Patients Included In 13 EORTC-Gimema-HOVON Leukemia Group Trials

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Abstract

Background Secondary acute myeloid leukemia (sAML) describes patients (pts) with a history of malignant or non-malignant disease or AML secondary to environmental, occupational or therapeutic exposures. They are generally associated with poor outcome despite the use of intensive treatments. The impact of clinical features and type of treatment on pts' outcome is still not well established. In the current analysis we evaluated sAML pts who were treated in 13 EORTC collaborative trials conducted between May 1986 and January 2008. sAML pts in the database were pooled to characterize clinical features of the disease and evaluate changes in survival over these years (yrs).

Method Main selection criteria were AML with bone marrows blasts ≥20% and documented history of prior malignancy, non-malignant disease and/or toxic exposure. AML-M3 and MDS without confirmed diagnosis ≥2 months before AML were excluded. All pts were eligible for standard treatment. Induction regimens were anthracycline and AraC based: 7+3, including etoposide, intensified with high dose (HD)-AraC randomized to standard doses (SD) in younger (AML12) or gemtuzumab ozogamicin in elderly pts. Consolidation regimens were age adapted. In mid-1980s, autologous transplant was tested vs a 2nd consolidation cycle (AML8A) in pts ≤45 yrs and thereafter used systematically in pts ≤60 yrs without available donor. Allogeneic transplant

(Allo-SCT) was offered to pts ≤46 yrs with HLA-compatible sibling since mid-1980s and expanded in the last decade to pts up to 59 yrs.

Selected pts were divided into 3 sAML cohorts, cohort A after MDS, cohort B after other malignant diseases and cohort C after non-malignant conditions and/or toxic exposure.

Results Of 8858 pts enrolled in the 13 evaluated studies, 962 were sAML. Median age was 63 yrs (range 16-85), 413 were young (≤60 yrs) and 549 were elderly (≥61 yrs); 54% were males. Cohort A consisted of 509 pts (median age 64 yrs), cohort B of 362 pts (median age 59 yrs) and cohort C of 91 pts (median age 61 yrs). In cohort B, breast cancer (24%) and lymphoma (14%) were the most frequent primary tumors. Autoimmune diseases represented 22% of non-malignant conditions.

In young pts, complete remissions (CR/CRi) rate was 59%; 55% in SD-AraC vs 89% in HD-AraC treated pts. Allo-SCT in CR1 was performed in 21% of all pts. The Allo-SCT rate increased from 5% before 1990, 20% in 1990-1999 to 25% from 2000 (20% in SD-AraC vs 31% of HD-AraC treated pts).

CR/CRi was achieved in 45% of elderly pts.

Median follow-up was 6 yrs. Median overall-survival (OS) was 14.5 months in young and 9 months in elderly pts. The 5-yr OS was 28% and 7% respectively. Five-yr OS was 11% in cohort A and 22% in both cohort B and C.

Treatment outcome of younger pts according to disease features and treatment type over time in cohort A and B are detailed in **table 1** & **2**. Using Cox model stratified by cohort age, gender, WBC, risk group, year of treatment and HD-AraC were independent prognostic factors for OS. In the AML12 study, compared to *denovo* pts, sAML pts ≤45 yrs had worse outcome if treated with SD-AraC whereas a better OS was seen if treated with HD-AraC.

Table1 View inline | View popup

Univariate analysis of OS for young **pts**

Table2 View inline | View popup

Multivariate analysis of OS for young **pts** in cohort A and B

In elderly pts only the good/intermediate risk group of cohort B had a relatively better 5-yr OS (15%).

Conclusions The outcome of sAML in younger pts has improved over the yrs in parallel with HD-AraC introduction in induction of remission. HD-AraC should be considered for younger pts with sAML.

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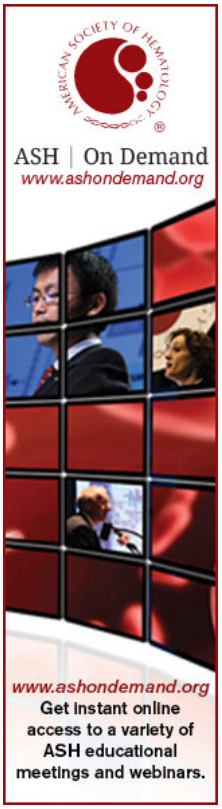

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