Reviewer’s report

**Title:** Clinical Characteristics and Outcomes of Patients with Acute Myelogenous Leukemia Admitted to Intensive Care: A Case-Control Study

**Version:** 2  **Date:** 10 May 2010

**Reviewer:** Utz Krug

**Reviewer’s report:**

The authors describe an analysis of 45 AML patients admitted to the ICU for any reason. Matching was performed with non-ICU AML patients by age and sex and with non-AML ICU patients for age, sex and APACHE II-score. While the selection of the parameters selected for matching might miss some important disease-specific differences between the AML-ICU and the AML-non-ICU cases, the applied statistical analysis is appropriate. Even though the authors perform a thorough analysis of these patients regarding intensive care scores and parameters, some important AML-specific parameters were neglected, as outlined below. The advantages of this study is a robust quantification of the incidence of ICU admissions in patients with newly diagnosed AML. However, because of the possible importance of the AML-specific parameters on the results and because of a presumably high heterogeneity of the non-AML ICU group, the conclusions from the comparisons of the different groups have to be taken with caution.

**Major compulsory revisions:**

Park HJ et al (Leuk Lymphoma 2008;49(10):1929–34) could demonstrate the status of the leukemia (relapsed / refractory versus other) being an independent adverse risk factor in AML patients admitted to ICU with septic shock, among the SOFA score. This possible influence of the remission status should also be evaluated in this manuscript. Considering the median hospital stay of 35 days in this cohort, a substantial percentage of patients might have had a response evaluation before ICU admission.

In addition, neutropenia and the estimated duration of neutropenia is an established risk factor for surviving infectious complications in AML. It therefore seems required to know whether both a severe neutropenia at the time of ICU admission and a prolonged neutropenia after ICU admission (>7 days) had an influence on the outcome of this cohort. Alternatively to the latter analysis, one could analyse the time from the start of induction therapy to ICU admission if the AML patients were treated comparably intensive.

The patients of the AML ICU and the AML non-ICU groups were not matched according to specific treatment. As the authors discuss, there is an inevitable potential bias in non-ICU patients who were precluded to ICU admission. How was the distribution of different therapeutic regimens in this patients, i.e. intensive induction therapy vs palliative cytoreductive therapy vs supportive care? If
differences exist, patients of the AML-ICU and the AML-non-ICU group have to be matched according to the type of treatment.

Minor essential revisions:

p. 9: 2nd paragraph: '....ICU controls when compared with either AML cases or controls' change to: '....ICU controls when compared with either AML ICU cases or AML non-ICU cases'

table 4: the comparison of G-CSF application and application of AML-specific chemotherapy during ICU does not make sense in the comparison of AML-versus non-AML-patients. In addition, the correct number is 'n.a.' (not applicable) in the corresponding non-AML controls instead of '0 (0)'. In addition, to get a comparison of the incidence of chemotherapy days, transfusions, antimicrobial therapy and G-CSF use, those parameters should be compared with the AML-non ICU group.

p15: The conclusion '...decisions about withholding life-sustaining measures in our study may have related to...' has to be taken with caution: first, except the SOFA score, none of the other parameters showed a significant difference between the patients with switch to DNR and the others. Second and more important, a possible change of the AML disease status during the ICU stay influencing the switch to DNR (i.e. reappearance of peripheral blood blasts, bone marrow assessment showing an inadequate treatment response) has not been taken into account. The conclusion should be modified accordingly.

p. 11: The statement 'Tremblay et al. reported that among 163 newly diagnosed AML...' is wrong, since the study by tremblay et al. included patients with AML of all stages of the disease, including patients receiving allogeneic hematopoietic stem cell transplantation (HSCT). This should be clearly stated, since an allogeneic HSCT places the patients to a higher risk for acquiring infectious complications than an induction therapy of a newly diagnosed AML.

The manuscript mentioned above (Park et al) should be cited

Discretionary Revisions

Procalcitonin has been established as a good predictor for the severity of an infection. Since the vast majority of AML patients admitted to ICU suffer from infectious complications, the procalcitonin level at diagnosis or after initial antimicrobial treatment might also be evaluated as a predictor for survival.

It is much easier to follow the references if the references in the manuscript and in the supplemental table had the same numbering

Key messages: The statement '...relatively few patients...' is subjective; one could also consider 11.7% of patients suffering from a life-threatening complication after therapy a relatively high portion.

The matching procedure of the AML-ICU group with the non-AML ICU groups included only sex, age and APACHE II-score. While the populations are well
matched by disease severity, as done by the APACHE II score, it is not clear what the differences in comorbidities in table 1 say. It might be that the 'comorbidities' were the underlying disease in many cases, as AML was for the AML-ICU group. To adjust for this, one could estimate the severity of underlying diseases by a comorbidity score. Alternatively, a table with the numbers of existing comorbidities per patient could be listed. It has to be clear. ly stated, however, that the ICU-non-AML group is a very heterogenous one and only limited conclusions can be drawn from a comparison with this group.

The studies leading to an approval of voriconazol in the prophylaxis of invasive fungal infections during induction therapy showed an improved overall survival in patients receiving antifungal prophylaxis during induction therapy. It could be discussed that the reported incidence of ICU admissions (from an era before vori prophylaxis) could be lower now with modern antifungal prophylaxis available.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests