Early matched sibling hematopoietic-cell transplantation for adult
AML in first remission using an age-adapted strategy: long-term results of a prospective GOELAMS study

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Running title : Age-adapted conditioning regimen for allogeneic hematopoietic stem cell transplantation for AML in first remission.

Keywords: Acute myeloblastic leukemia, allogeneic hematopoietic cell transplantation
ABSTRACT

The GOELAMS LAM2001 phase III trial, involving 832 patients with acute myeloid leukemia (AML) (median: 46 years, range: 17-60) proposed HLA-identical sibling allograft of hematopoietic stem cells (HSCT) for all patients with an identified donor. The trial compared reduced intensity conditioning (RIC) for patients over 50 years of age (N=47) and myeloablative conditioning for younger patients (N=117). Bone marrow HSCT was performed in the younger patients, while the older ones received a consolidation course, followed by peripheral blood allo-HSCT using RIC. The incidence of grade II-IV aGVHD, was 51.9% (95% CI:42.1-61.8) and 11.3% (1.6-21.2) after myeloablative or RIC respectively (p<0.0001) and that of cGVHD 45.8% (95% CI: 34.8-56.7) and 41.7% (24.7-58.6) (NS). Cumulative incidence (CI) of non-relapse mortality at 108 months was 15.8% (95%CI: 9.8-23.2) for myeloablative, and 6.5% (0.2-16.2) for RIC (NS). CI of relapse at 108 months was 21.7% (95%CI: 13.9-28.6) and 28.6% (16.5-43.4) (NS). Overall survival at 108 months was 63.4% (95%CI: 54.6-72.2) and 65.8% (52.2-72.2) respectively after myeloablative or RIC (NS). RIC PBSC allo-HCT is prospectively feasible for patients aged between 51 and 60 without excess of relapse or non-relapse mortality and compares favorably with myeloablative marrow allo-HCT proposed to younger patients.

This study was registered at http://clinicaltrials.gov/ct n° NCT01015196
INTRODUCTION

Great progress has been achieved, since the introduction of aracytine and anthracyclins, in the initial management of patients with acute myeloid leukemia (AML), and complete remission (CR) rates have considerably improved, most failures being attributable to early death rather than induction toxicity. However, the rate of relapse remains unacceptable, and new strategies are required to improve the long-term outcome of AML patients. Part of the progress relies in post-remission chemotherapy but hematopoietic stem-cell transplantation (HST) is another opportunity to consider, be it autologous or allogeneic, the latter with related or unrelated donors.

In the recent years, the GOELAMS' group has indeed developed risk-adapted strategies to improve the outcome of patients with AML in first remission. The trial reported here, designed in 2001, tested different strategies in relation to HST. For patients lacking geno-identical donors, one aim was to compare intensive consolidation followed by one or two autologous peripheral stem cell transplantation. For patients with a sibling donor, the second aim proposed an early allo-HST with an age-adapted conditioning regimen. A myeloablative regimen was applied for patients less than 50 years of age. For patients between 50 and 60 years of age, a reduced-intensity conditioning (RIC) regimen was applied after an early intensification and before allo-HST.

The results of the allogeneic HST arm of this trial are presented here, showing that this strategy yielded similar results in the two age groups.
PATIENTS AND METHODS

Patient eligibility

From November 2001 to April 2005, 832 previously untreated patients (age ≤ 60 years) with AML, issued from 28 centers, were enrolled in the LAM-2001 GOELAMS study. Patients with AML3 or isolated extramedullary disease, as well as patients with a previous diagnosis of myelodysplastic or myeloproliferative disorder were excluded. Patients were also excluded from the study if they were considered ineligible to receive the planned treatment (WHO ECOG status ≥ 3, severe arrhythmia, progressive coronary artery disease, acute heart failure, or left ventricular ejection fraction < 40%, renal or liver dysfunction, psychiatric disease, or inadequate familial support). All patients underwent diagnostic bone marrow aspiration with evaluation of morphology (≥ 20% blasts), immunophenotyping, cytogenetics. Whenever possible sampling for molecular testing (\textit{FLT-ITD/D835, NPM, CEBPα}) was performed at diagnosis. Cytogenetic analyses were performed according to the International System for Human Cytogenetic Nomenclature (ISCN)\textsuperscript{4}. Three prognostic groups were defined: 1) \textit{low risk}: t(8;21)(q22;q22), inv(16)(p13q22); 2) \textit{high risk}: complex abnormalities (≥ 3), del(5q), -5, -7, 3q rearrangements, t(9;22), t(6;9), 11q23/\textit{MLL} rearrangements except t(9;11); 3) \textit{intermediate risk}: all other cases. HLA-typing was performed as early as possible after diagnosis.

In accordance with the Declaration of Helsinki, the study was reviewed and approved by the ethics committee (Nantes, France; ID 2000/5/00) and all patients provided written informed consent prior to their participation to the study in accordance with the Declaration of Helsinki.
Study Design

The treatments applied have been extensively described elsewhere.3 Briefly, after inclusion, all patients were randomized to receive induction chemotherapy with either daunorubicin, 60 mg/m² on days 1 to 3, or idarubicin, 8 mg/m² on days 1 to 5, associated with continuous infusion of cytosine-arabinoside (ara-c), 200 mg/m² on days 1 to 7. Response assessment was performed on day 15. If less than 5% bone marrow blasts were present, no additional chemotherapy was prescribed and evaluation for complete remission was performed between d28 and d35. If there were more than 5% blasts in the bone marrow, a second induction course was given including daunorubicin 35 mg/m² or idarubicin 8 mg/m² on days 17 and 18, according to initial randomization and ara-c 1000 mg/m² bid on days 17 to 20, followed by G-CSF (lenograstim). Patients in CR could proceed to further steps of the trial according to the identification or not of an HLA-identical sibling, at diagnosis or second randomization. Patients not in CR could receive one additional induction course similar to the first intensive consolidation course (ICC) and were excluded from the protocol if not in CR after this.

Patients without a donor proceeded to second randomization in order to receive one (arm A) or two (arm B) autologous hematopoietic cells transplantation (auto-HCT), as late consolidation course(s). Results of this part of the study have been reported elsewhere.3

Patients with an HLA-identical sibling donor were planned to receive an allo-HCT. If less than 51 years old, they received bone marrow allogeneic stem cell
transplantation after a myeloablative conditioning regimen consisting of cyclophosphamide (120 mg/kg over 2 days) and total body irradiation (6 fractions of 2 Gy) Graft-versus-host disease (GVHD) prophylaxis included a combination of cyclosporin (CSA) and a short course of methotrexate (15 mg/m² on D+1; 10 mg/m² on D+3 and D+6). A mini-consolidation course (daunorubicin 60 mg/m² or idarubicin 12 mg/m² for 2 days, ara-c 100 mg/m² SQ for 7 days) was administered to allow planning of the transplant procedure. Patients over 51 years of age received a mini-consolidation as previously described, followed by one ICC (daunorubicin 60 mg/m2 or idarubicin 12 mg/m² for 2 days, ara-c 3 g/m² IV x 2 / D for 4 days) before peripheral blood stem cell (PBSC) transplantation after reduced intensity conditioning (RIC), combining oral busulfan, 8 mg/kg over 2 days, fludarabine, 120 mg/m² over 4 days, rabbit anti-thymocyte globulins (ATG, Genzyme) 2,5 mg/kg on D-4 and D-3 and GVHD prophylaxis with CSA alone.

**Statistical methods**

Descriptive statistics are reported as frequencies, or medians and range. Normality of samples’ distribution was checked with the Kolmogorov-Smirnov test. Comparisons of median values were performed using the Mann and Whitney rank sum test. The chi-squared test or Fisher’s exact test were used to test for differences between groups. Statistical analysis was performed on an intention to treat basis using Medcalc software (Mariakerke, Belgium). Outcome data were updated at the date of September 11, 2008. Overall survival (OS) was calculated from the date of the first randomization until the date of death from any cause, with censoring of other patients at the date of last follow-up. Leukemia
free survival (LFS) was calculated from the date of first CR until the date of relapse or death of any cause. For patients who did not relapse, observation was censored on the date of last follow-up. Survival data except cumulative incidences were estimated by the Kaplan-Meier method, then compared by the log-rank test, with hazard ratio (HR) estimated by the Cox model. Factors associated with a significant impact in univariate analysis were retained for multivariate logistic regression. Type 1 error was fixed at the 5% level. All tests were two-tailed. Failure events as relapse and deaths from causes related to the transplant were calculated performing competing risk analysis using the R software (R foundation for statistical computing).5

RESULTS

Patient and transplantation characteristics

Between November 2001 and April 2005, a total of 832 patients were included in the study.3 Nine patients were considered ineligible, 8 with a wrong diagnosis or age (2 older than 60, one AML3, and 5 Ph+ CML in acute phase). One patient was excluded because he died before receiving chemotherapy. There was no significant difference between the two groups (idarubicin n=412 or daunorubicin, n=411) of the first randomization regarding initial characteristics4. Of the 823 patients evaluable for induction treatment, 676 (82%) achieved a CR, including 579 patients treated with one course of chemotherapy (86 % of CR patients). There were 24 (2.9%) early deaths, 12 (1.4%) deaths during aplasia, 7 (0.8%) deaths after hematologic recovery and 104 (12.6%) patients with induction failure. The CR rate was not significantly different between the two induction treatment arms (idarubicin 83% vs daunorubicin 81%, NS).
Out of 676 patients in CR, 640 were assigned to the intensive treatment as scheduled by the trial. The 36 remaining patients were not considered for intensive post remission therapy for the following reasons: extrahematologic toxicity (5), protocol violation (17), refusal (4), early relapse (10). Among these 640 patients, 410 had no sibling donor identified and were eligible for the second randomization: they were assigned to receive one (arm A, n = 206) or two (arm B, n = 204) courses of auto-SCT. Two hundred and thirty patients had an HLA identical sibling donor. Of them, 29 with good prognosis and in CR1 after one induction were assigned to receive 2 courses ICC, while 201 were eligible for an allograft. Out of them, 10 left the study early before scheduling transplant (relapse 1, major early toxicities 4, major protocol violations 5).

No significant differences were observed between patients having or not a sibling donor; the only difference between patients assigned to receive an allograft being age as per protocol. The median age and follow-up for patients assigned to receive auto-SCT (n=410) were 46 years old (range: 17-60) and 53 months (range: 9-83), respectively. For patients with a sibling donor they were 44 years old (range: 17-60) and 53 months (range: 9-83), respectively.

Finally, of the 191 patients with an identified HLA-identical sibling donor, 164 were effectively transplanted according to the planned strategy in first remission. The remaining 27 patients could not receive the planned allo-HCT for the following reasons: patient’s refusal (N=2), donor’s refusal (N=2), relapse (N=11), non-leukemic deaths (N=2), protocol violation, including two cord blood transplants (N=6), poor performance status (N=3) and one donor’s exclusion. Of the 164 transplanted, 117 received a myeloablative regimen and 47 a reduced intensity regimen. Patients’ characteristics between the two groups (Table 1)
were comparable, except that there were more male patients in the myeloablative group (p=0.02), more older patients requiring two courses of chemotherapy to achieve CR (p=0.03) and, as expected by the protocol, older age for RIC. Nine patients eligible for the myeloablative regimen were conditioned with RIC and two patients aged 56 and 52 eligible for RIC were treated with a myeloablative regimen.

Gender mismatches were 17 female/male, 27 male/female in the myeloablative arm and 16 female/male, 7 male/female in the RIC arm (p=0.03).

**Transplantation outcomes (Table 2):**

**GVHD**

Among patients receiving a myeloablative conditioning, 56 developed acute GVHD (grade I n=10, grade II n=32, grade III n=10, grade IV n=4) and 34 chronic GVHD, extensive in 20 cases. Within the group of patients conditioned with RIC, 12 developed acute GVHD (grade I n= 6, grade II n=2, grade III n=2, grade IV n=1, unknown, n=1) and 16 chronic GVHD, extensive in 5. The overall incidence of grade II-IV acute GVHD, was 51.9% (95% CI: 42.1-61.8) and 11.3% (95% CI: 1.6-21.2) for myeloablative and RIC respectively (p<0.0001) and for chronic GVHD 45.8% (95% CI: 34.8-56.7) and 41.7% (95% CI: 24.7-58.6) (p=0.83).

**Non-relapse mortality**

The cumulative incidence of NRM at 36 months was 12.9% (95% CI: 7.6-19.7) for myeloablative conditioning and 4.2 % (95 % CI: 0.7-12.9) for RIC. With a longer follow-up at 108 months, these figures were 15.8% (95% CI: 9.8-23.2) and
6.5% (95% CI: 0.2-16.3) respectively (NS). All but two non-relapse deaths were due to treatment related toxicities.

**Relapse**

The cumulative incidence of relapse at 36 months was 18.9% (95% CI: 12.4-26.6) for myeloablative conditioning and 20.7% (95% CI:15.7-41) for RIC and at 108 months, 21.7 % (95% CI: 13.9-28.6) and 28.6% (95% CI:16.5-43.4) respectively (NS).

**Survival**

The overall survival at 108 months, after allo-HST of patients in first complete remission was 68 % (95% CI : 59.3-76.3) and 69.3% (95% CI : 55.6-82.1) respectively after myeloablative conditioning or RIC (NS). This analysis only considered patients who received an allo-SCT. On an intent-to-treat basis, results were not statistically different (p=0.35).

Event-free survival at 108 months was 63.4 % (95% CI : 54.6-72.2) and 65.8 % (95% CI : 52.2-79.1) respectively (NS). On an intent to treat basis, results were still not different between the two arms (p=0.23).

**Comparison of auto -and allo-HST arms outcome**

As reported before\(^3\), similar outcomes were observed in this trial between allo-SCT patients and those, without related donor, who received one or two auto-HST. In an intent to treat analysis, and considering only those with intermediate
or high risk cytogenetics, allo-SCT (RIC or myeloablative) did not reach significantly better EFS and OS than auto-SCT (p=0.23 and 0.29 respectively).

**DISCUSSION**

The results reported for this LAM-2001 trial of the GOELAMS group indicate that, in a prospective multicentric study, allo-HCT performed in early first remission may yield comparable results for unselected older patients, conditioned with RIC, and for younger patients conditioned with a myeloablative regimen.

It must be pointed that the study, initiated before 2001, did not include NPM1/FLT3 molecular studies, and retrospective analysis has only been possible for 37 allografted patients with a normal karyotype (16 patients with NPM1+/FLT3-ITD)\(^6\). The possible impact of this prognosis factor therefore cannot be appreciated here. Moreover, good prognosis patients characterized by AML without hyperleucocytosis and CBF cytogenetics (inv16, t(8;21)) in remission after the first induction course, were excluded from the study.

Numerous reports have described retrospective results of RIC HST for older AML patients, often with more advanced diseases or heterogeneous initial chemotherapies.\(^7-13\) This cohort of unselected patients, treated prospectively, has however several points of interest including the fact that two different sources of hematopoietic stem cells were used yet yielded similar results. Within the smaller group of older patients, aged between 50 and 60 years old, the probability of relapse was similar to that of the younger patients conditioned with myeloablative regimen, even including ATG. Significantly less acute GVHD were observed after
RIC but, in this trial no statistical difference was observed for the incidence of chronic GVHD. As this trial was designed in an era where the natural history of GVHD after reduced intensity conditioning was not fully appreciated, late acute GVHD were probably partly included in the chronic group. However, the low incidence of chronic GVHD among the older patients suggests that, overall, the incidence of GVHD was still lower in this subgroup of patients.

Even without statistical difference in terms of NRM (p=0.12), there was a trend for increased toxicity after myeloablative regimen, as observed in other settings.\(^{14,15}\) However, direct comparison of the two transplantations approaches would be biased in this trial, since older patients received more intense chemotherapy prior to the procedure than patients of the younger group who were conditioned without intensive course after the mini-consolidation. In this older group, a potent graft-versus-leukemia effect is suggested after RIC, probably associated with an optimal leukemic burden reduction prior to transplantation. The upper age limit of 60 is certainly insufficient today to confirm a definite improvement for “older” patients and complementary strategies are needed to evaluate this approach. This question remains unsolved since the 90’s and is discussed regularly.\(^{16,17}\) Strategies in allogeneic stem cell transplantation are evolving with time and numerous approaches of conditioning regimen are still under study, as well as new immunosuppressive combinations for the prevention of GVHD, thus complicating comparisons. In this study, the use of ATG was probably beneficial to lower toxicities and did not result in a significant increase in the probability of relapse. The availability of IV busulfan, which is largely used in current studies, will probably help to further decrease morbidity.
If this trial is confirmed and a prospective feasibility is proven to include allo-HCT in the strategy for older high-risk patients, the question remains of what will be the upper age limit for the next decade. Another pending question is that of the best donor’s source to be chosen without increasing NRM. Here, it is interesting to note that similar results were obtained using either bone marrow or PBMC, but the best source of cells remains to be determined. Another possible source to better explore is that of cord blood. Of note, both the patients excluded from this report because they received such HST died, one 7 months and the other one 29 months after HST, the second one in relapse.

Other promising immunotherapeutic approaches have also been recently developed for the intensification regimen in older patients, such as infusion of mismatched stem cells after chemotherapy, but results need to be confirmed and balanced with allo-HCT.

In conclusion, in this trial, long-term disease control of adult AML using RIC allo-HCT for older patients compared favourably with a younger group of patients conditioned more intensively in a prospective manner.
Conflict of interest disclosure:
The authors declare no competing financial interests.

Authorships:
BL, NI, AP, JLH and JYC wrote the protocol
BL, JYC analyzed data, recruited patients, provided clinical care, performed bibliographic search and wrote the manuscript.
MCB performed data collection management, validation and statistical analyses and wrote the manuscript.
LF helped for performing data collection
IL, OB and PCL produced and validated cytogenetic and molecular data.
BL, AP, AH, MD, NF, DB, BW, PC, JC, MC, MH, FL, TL, ER, MOU, CB, DB, JLH, NI, and JYC recruited patients, and provided clinical care.

Acknowledgments
We acknowledge Nicole Raus from the SFGM-TC and the numerous ARCs and TECs who helped with data collection and monitoring, especially Roselyne Delepine and Cindy Grandjenette.
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Table 1
Characteristics of the overall cohort of patients who effectively received allogenic stem cell transplantations

<table>
<thead>
<tr>
<th>Patients</th>
<th>Allogeneic HCT N=164</th>
<th>Myeloablative N=117</th>
<th>RIC N=47</th>
<th>P***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up for alive patients (range)</td>
<td>88 months (16-119)</td>
<td>88 months (30-119)</td>
<td>88 months (16-119)</td>
<td>NS</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>44 years (17-60)</td>
<td>39 years (17-50)</td>
<td>54 years (34-60)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>84 (51%)</td>
<td>67 (57%)</td>
<td>17 (36%)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>Previous solid tumor</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Performance status:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>151 (92%)</td>
<td>108 (92.3%)</td>
<td>43 (91.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>13 (8%)</td>
<td>9 (7.7%)</td>
<td>4 (8.5%)</td>
<td></td>
</tr>
<tr>
<td>Median initial WBC count (range)</td>
<td>11.8 G/L (0.7-308)</td>
<td>12.6 G/L (0.7-308)</td>
<td>9.3 G/L (1-159)</td>
<td>NS</td>
</tr>
<tr>
<td>FAB classification (0/1/2/4/5/6/7)</td>
<td>8/37/36/29/13/5/0</td>
<td>5/29/25/21/12/4/0</td>
<td>3/8/11/8/1/1/0</td>
<td>NS</td>
</tr>
<tr>
<td>Not classified</td>
<td>36</td>
<td>21</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Karyotype</td>
<td></td>
<td></td>
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<tr>
<td>Not evaluable</td>
<td>2 (1.2%)</td>
<td>1 (0.8%)</td>
<td>1 (2.1%)</td>
<td></td>
</tr>
<tr>
<td>Failure</td>
<td>12 (7.3%)</td>
<td>10 (8.5%)</td>
<td>2 (4.3%)</td>
<td></td>
</tr>
<tr>
<td>Partial failure</td>
<td>7 (4.2%)</td>
<td>6 (5.2%)</td>
<td>1 (2.1%)</td>
<td></td>
</tr>
<tr>
<td>Evaluable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable (1)</td>
<td>18 (10.9%)</td>
<td>14 (12%)</td>
<td>4 (8.5%)</td>
<td></td>
</tr>
<tr>
<td>Intermediate(2)</td>
<td>101 (61.5%)</td>
<td>72 (61.5%)</td>
<td>29 (61.7%)</td>
<td></td>
</tr>
<tr>
<td>High-risk (3)</td>
<td>24 (14.6%)</td>
<td>14 (12%)</td>
<td>10 (21.3%)</td>
<td>NS</td>
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</tbody>
</table>

**First randomization**

<table>
<thead>
<tr>
<th>Drug</th>
<th>88 (53.6%)</th>
<th>59 (50.4%)</th>
<th>29 (61.7%)</th>
<th>NS°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daunorubicin</td>
<td>76 (46.3%)</td>
<td>58 (49.6%)</td>
<td>18 (38.3%)</td>
<td></td>
</tr>
</tbody>
</table>

**Complete remission**

| CR in one course | 120 (73.2%) | 87 (74.3%) | 33 (70.2%) | P=0.03 |
| CR in two courses | 44 (26.8%) | 30 (25.7%) | 14 (29.8%) |    |

**Donor-recipient CMV serostatus**

| +/+               | 44 (26.8%) | 26 (22.2%) | 18 (38.3%) |    |
| +/-              | 22 (13.4%) | 17 (14.5%) | 5 (10.6%) |    |
| -/+            | 26 (15.9%) | 15 (12.8%) | 11 (23.4%) |    |
| -/-           | 65 (39.6%) | 52 (44.4%) | 13 (27.7%) | P=0.04 |
| Missing        | 7 (4.3%) | 7 (6%) | 0 |   |

**Donor-recipient sex match**

| Male-male | 43 (26.2%) | 29 (24.8%) | 14 (29.8%) |    |
| Male-female | 34 (20.7%) | 27 (23%) | 7 (14.9%) |    |
| Female-male | 33 (20.1%) | 17 (14.5%) | 16 (34%) | P=0.03 |
| Female-female | 6 (3.7%) | 6 (5.1%) | 0 |    |
| Missing | | | |   |

**Type of donor**

| HLA-identical sibling | 162 (98.8%) | 115 (98.3%) | 47 (100%) |
| Mismatched Relative | 2 (1.2%) | 2 (1.7%) | |   |

Abbreviations: WBC: white blood cell. FAB: French-American-British; CR: complete remission; Karyotype: (1): t(8;21) or inv(16), (3) high-risk: -5, 5q-, -7, 3q abnormalities, t(6;9), multiple abnormalities (more than five abnormalities), (2) all other chromosomal abnormalities.
Table 2
Clinical evolution of allo-SCT recipients in the myeloablative and RIC arms of the trial shows similar evolution except for the higher incidence of acute GVHD in patients receiving a myeloablative conditioning regimen.

<table>
<thead>
<tr>
<th></th>
<th>Myeloablative</th>
<th>RIC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute GVHD grade II-IV % (95% CI)</td>
<td>51.9 (42.1-61.8)</td>
<td>11.3 (1.6-21.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic GVHD* % (95% CI)</td>
<td>45.8 (34.8-56.7)</td>
<td>41.7 (24.7-58.6)</td>
<td>NS (0.83)</td>
</tr>
</tbody>
</table>

Cumulative incidence
of NRM % (95% CI)
36 months | 12.9 (7.5-19.7) | 4.2 (0.7-12.9) | NS (p=0.33)*
72 months | 15.8 (9.8-23.2) | 6.5 (0.2-16.2) |
108 months | 15.8 (9.8-23.2) | 6.5 (0.2-16.2) |

Cumulative incidence
of relapse % (95% CI)
36 months | 18.9 (12.4-26.6) | 20.7 (15.7-41) | NS (0.33)
72 months | 21.7 (13.9-28.6) | 28.6 (16.5-43.4) |
108 months | 21.7 (13.9-28.6) | 28.6 (16.5-43.4) |

EFS % (95% CI)
36 months | 68.1 (59.5-76.4) | 68.1 (54.6-80.9) |
72 months | 63.4 (54.6-72.2) | 65.8 (52.2-72.2) | NS (p=0.83)
108 months | 63.4 (54.6-72.2) | 65.8 (52.2-72.2) |

OS % (95% CI)
36 months | 73.4 (65.2-81.1) | 76.2 (63.1-87.3) |
72 months | 68 (59.3-76.3) | 69.3 (55.6-82.1) | NS (p=0.82)
108 months | 68 (59.3-76.3) | 69.3 (55.6-82.1) |
Figure 1: Overall survival post allogenic stem-cell transplantation shows similar outcome in the two age groups and conditioning regimen.
Figure 2: Myeloablative and RIC estimated cumulative incidence curves with non relapse-mortality and relapse as competing events show similar outcome in the two age groups with adapted conditioning regimen.
Early matched sibling hematopoietic-cell transplantation for adult AML in first remission using an age-adapted strategy: long-term results of a prospective GOELAMS study

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