Unrelated matched versus autologous transplantation in adult patients with good and intermediate risk acute myelogenous leukemia in first molecular remission

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Abstract
Patients with Acute Myelogenous Leukemia have a better outcome if reaching molecular remission. We compared the outcome of 373 patients autografted and 335 patients allografted with a 10/10 compatible unrelated donor in first molecular remission. Patients were stratified using the ELN European Leukemia Net classification. ELN favorable group: (234 auto and 70 unrelated transplants). By univariate analysis, in the auto group, the Non Relapse Mortality (NRM) was lower (3.7% versus 19%; \( P < 10^{-24} \)), Relapse Incidence (RI) higher (29% versus 17%, \( P < 10^{-24} \)), Leukemia Free Survival (LFS) identical (67% versus 64%) and Overall Survival (OS) better than in the allogeneic group (83% versus 62%; \( P < 0.008 \)). By multivariate analysis, unrelated donor was superior to autologous transplantation for LFS (HR: 0.36, \( P < 10^{-25} \)) and OS (HR: 0.53, \( P < 0.01 \)).

ELN intermediate group 2: (52 autologous and 93 unrelated donors). The outcome was identical. We conclude that good risk patients get higher benefit from autologous transplantation. Intermediate risk 2 patients have the same outcome and Intermediate risk 1 patients get higher benefit from unrelated donor transplants.

1 | INTRODUCTION

Several studies have shown that adult patients with Acute Myelogenous Leukemia (AML) have a better outcome if they reach a status of non detectable minimal residual disease (MRD negative). In these studies, MRD negativity (or non detectability) has been assessed either by
immunophenotyping using 8 or even ten colors\textsuperscript{1,2} or when a molecular marker exists, by molecular biology,\textsuperscript{3} defining molecular remission (molecular CR). In all studies, MRD negativity was strongly correlated with better outcome, whatever the sampling time point considered, be it after induction, after consolidation,\textsuperscript{4,5} pre\textsuperscript{6} and post allogeneic stem cell transplantation.\textsuperscript{7–13}

The number of studies evaluating MRD negativity as a prognostic factor in autografted patients is limited but likewise, adult patients with AML autografted in first molecular remission (molecular CR1) evaluated by WT1 overexpression\textsuperscript{14} have a lower Relapse Incidence (RI) post transplant and a better Leukemia Free Survival (LFS). Retrospective EBMT registry studies have also suggested that Autologous Stem Cell Transplantation (ASCT) might bring more benefit to chemo sensitive patients of the good and possibly intermediate risk groups, and more generally those autografted in molecular CR.\textsuperscript{15,16}

A recent EBMT study compared allogeneic transplantation (HSCT) with unrelated donors to ASCT in CR1\textsuperscript{17}: it showed that full matched but not one antigen mismatched UD transplant was associated with a better LFS than ASCT; the Overall survival (OS) was however similar in the two groups. This study did not consider patients in molecular CR1.

We therefore decided to use the EBMT registry to select non high risk AML patients transplanted in molecular CR1 to compare the two transplant modalities in this better prognosis/chemosensitive patient population.

2 METHODS

This study is a retrospective, multicenter analysis. Data were provided by the Acute Leukemia Working Party (ALWP) of the EBMT group registry. The EBMT registry is a voluntary working group of more than 500 transplant centers that are required to report all consecutive stem cell transplantsations and follow-ups on an annual basis. Audits are routinely performed to ensure the accuracy of data. Since 1990, registry patients provided informed consent authorizing the use of their personal information for research purposes. The ALWP of the EBMT group approved this study.

Eligibility criteria for this analysis included adult AML patients (age ≥18 years), all with available cytogenetics, receiving either autografted (373) or allotransplanted with a full matched (10/10 identical) unrelated donor (335) while in molecular CR1 between January 2005 and December 2015. Patients with M3 AML were excluded from the analysis.

2.1 Statistical analysis

The primary end points of this study were Leukaemia-Free Survival (LFS) and Overall Survival (OS) at two years post transplant. Secondary endpoints included disease Relapse Incidence (RI) and Non-Relapse Mortality (NRM). Overall survival (OS) was defined as the time between the date of transplant and death. Leukaemia-free survival (LFS) was defined as survival without relapse.

Cumulative incidences of RI and NRM were calculated from the date of transplant to the date of relapse or death in remission, respectively, with the other event being the competing risk. LFS was defined as the interval from transplant to either relapse or death in remission. Follow-up values reported correspond to patients alive when the analysis was performed.

Patients were stratified using the 2010 ELN classification which takes into account cytogenetics and the presence of molecular markers, FLT3-ITD and NPM1 mutation in particular.\textsuperscript{18,19} All analyses were performed separately in the three following groups: favorable, intermediate 1 and intermediate 2. The status of molecular CR was defined locally by each team for each individual patient in relation to the presence of a specific molecular marker and according to the molecular quantification method in use at each local institution.

The main characteristics at diagnosis and at transplantation were compared between ASCT and UD 10/10 groups using. Mann–Whitney tests for quantitative variables, Chi-square test or Fisher exact test for categorical variables.

Univariate comparisons were done using the log-rank test for OS, LFS, and the Gray’s test for RI and NRM. Multivariate analyses were performed using Cox proportional hazards model for all endpoints. To avoid confounding factors, all factors with different distribution between the 2 types of transplant and factors known as potentially related to the outcome were included in the final regression model, and we did not proceed to any variable selection. All tests were two-sided. The type I error rate was fixed at 0.05 for determination of factors associated with time to event outcomes. To test for a centre effect, we introduced a random effect or frailty for each centre into the model.\textsuperscript{20,21}

Statistical analyses were performed with SPSS 22.0 (IBM Corp., Armonk, NY, USA) and R 3.2.3 software packages (R Development Core Team, Vienna, Austria).

3 RESULTS

The follow up of alive patients was 35 months in the autograft group and 23 months in the UD10/10 allo group.

Supporting Information Table S1 describes the two patient populations. In the autograft group, peripheral blood was more often used as a stem cell source (96% versus 76%, \(P < 10^{-4}\)) than in the UD group. The proportion of patients with a FLT3-ITD was higher in the UD group (68.8% vs. 31.9%; \(P < 10^{-4}\)). The pretransplant regimens were standard for the majority of patients: in the ASCT group, 181 patients received a combination of Busulfan and Cyclophosphamide (BUCY) and 52 a combination of Busulfan and Melphalan (BUEML). For UD transplants, 165 patients (50%) received a myeloablative regimen (MA), including 65 BUCY and 38 BU+ Fludarabine (BULFU) and 166 a reduced intensity conditioning (RIC) (50%) including in 82 the combination of BUFLU at lower dosages.

3.1 ELN favorable group

234 patients were autografted and 70 allografted (45 MA and 24 RIC, 1 missing) (Supporting Information Table S2). Patients allografted had a longer interval from diagnosis to transplant (185 versus 153 days, \(P < 10^{-4}\)).
By univariate analysis, in the ASCT group, the Non Relapse Mortality (NRM) was lower (3.7% versus 19%; \( P < 10^{-12} \)), the Relapse Incidence (RI) higher (29% versus 17%, \( P = .02 \)), the LFS not significantly different (67% versus 64%) and the OS better than in the UD group (83% versus 62%; \( P < 10^{-10} \)). By multivariate analysis (Table 1), age was significant for OS (HR: 1.46, CI 1.16-1.84; \( P = .001 \)) and ASCT was associated with a better OS than UD transplant (HR: 2.08, CI 1.05-4.13; \( P = .036 \)) (see Figure 1, insert 1A and 1B).

### 3.2 | ELN intermediate group 1

87 patients were autografted and 172 allografted (69 MA and 100 RIC, 3 missing) (Supporting Information Table S3). Allografted recipients had a higher proportion of FLT3ITD (83% versus 66%, \( P = .001 \)) and NPM1 mutations (62% versus 35%, \( P < 10^{-24} \)). By univariate analysis, in the ASCT group, the RI was higher (59% versus 18%, \( P < 10^{-10} \)) the Non Relapse Mortality (NRM) lower (2.5% versus 11.8%; \( P = .03 \)) and the LFS not significantly different (67% versus 64%). By multivariate analysis (Table 1), age was significant for OS (HR: 1.46, CI 1.16-1.84; \( P = .001 \)) and ASCT was associated with a better OS than UD transplant (HR: 2.08, CI 1.05-4.13; \( P = .036 \)) (see Figure 1, insert 1A and 1B).

### Table 1 | Multivariate analysis of prognostic factors in the ELN good genetic group

<table>
<thead>
<tr>
<th></th>
<th>RI</th>
<th>NRM</th>
<th>LFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favourable group</td>
<td>HR CI P</td>
<td>HR CI P</td>
<td>HR CI P</td>
<td>HR CI P</td>
</tr>
<tr>
<td>UD 10/10 vs. Auto</td>
<td>0.53 0.24-1.18 .12</td>
<td>3.98 1.32-11.98 .013</td>
<td>0.93 0.5-1.72 .81</td>
<td>2.08 1.05-4.13 .036</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.16 0.97-1.4 .11</td>
<td>1.14 0.78-1.65 .5</td>
<td>1.16 0.98-1.38 .09</td>
<td>1.46 1.16-1.84 .001</td>
</tr>
<tr>
<td>Year of Transplant</td>
<td>1.01 0.92-1.11 .80</td>
<td>1.22 0.99-1.51 .07</td>
<td>1.04 0.96-1.14 .33</td>
<td>1.05 0.93-1.17 .44</td>
</tr>
<tr>
<td>Time diag-T (mo)</td>
<td>1.02 0.96-1.08 .49</td>
<td>1.04 0.96-1.14 .32</td>
<td>1.03 0.98-1.08 .24</td>
<td>1.03 0.98-1.09 .27</td>
</tr>
<tr>
<td>PB vs. BM</td>
<td>1.41 0.51-3.87 .51</td>
<td>0.76 0.23-2.54 .65</td>
<td>1.16 0.53-2.53 .72</td>
<td>1.09 0.46-2.56 .86</td>
</tr>
<tr>
<td>Center</td>
<td>.24 .96 .18 .32</td>
<td>.24 .96 .18 .32</td>
<td>.24 .96 .18 .32</td>
<td>.24 .96 .18 .32</td>
</tr>
</tbody>
</table>

ASCT compared with UD transplants is associated with lower NRM and better OS.

### Figure 1

Outcome of AML patients transplanted in first molecular remission with autologous stem cells or stem cells from a 10/10 compatible unrelated volunteer donor. Leukemia Free Survival (A) and Overall Survival (B). 1:Favorable genetic group. 2:Intermediate 1 genetic group. 3: Intermediate 2 genetic group
lower (39% versus 70%; \( P < 10^{-5} \)) and the OS lower than in the UD group (61% versus 74%; \( P = .005 \)). By multivariate analysis (Table 2), UD rather than ASCT, was a significant favorable prognostic factor for both LFS (HR: 0.36, 0.24-0.56; \( P < 10^{-5} \)) and OS (HR: 0.53, 0.33-0.85; \( P = .01 \)) (See Figure 1, insert 2A and 2B).

### 3.3 | ELN intermediate group 2

52 patients were autografted and 93 allografted (51 MA and 42 RIC) (Supporting Information Table S4). There was no significant difference between ASCT and UD outcome for RI (36% versus 24%, \( P = .22 \)), LFS (60% versus 64%, \( P = .8 \)) and OS (74.5% versus 70.6%, \( P = .94 \)) (See Figure 1, insert 3 A and 3B). By multivariate analysis (Table 3) UD was associated with a higher NRM (HR: 6.1, CI 1.18-10.7; \( P = .01 \)) and OS (HR: 0.53, 0.33-0.85; \( P = .01 \)) (See Figure 1, insert 2A and 2B). Age was the only other significant factor in multivariate analysis for LFS (HR: 0.71, CI 0.36-1.42; \( P = .33 \)) and OS (HR: 6.12, CI 1.18-31.6; \( P = .03 \)).

### 4 | DISCUSSION

In a recent study on the prefered type of postremission therapy (PRT) in patients with AML in CR1, the HOVON/SAKK group reported results of a time-dependent multivariable analysis of allogeneic hematopoietic stem cell transplantation (alloHSCT) \( (n = 337) \) versus chemotherapy \( (n = 271) \) or ASCT \( (n = 152) \) in 760 patients aged 40-60 years with AML in CR1.\(^{22} \) Patients receiving alloHSCT showed improved overall survival (OS) as compared with chemotherapy (respectively, 57 ± 3% vs. 40 ± 3% at 5 years, \( P < .001 \)) and comparable OS was observed following alloHSCT and ASCT in patients with intermediate-risk AML (60 ± 4 vs. 54 ± 5%). However, alloHSCT was associated with better relapse-free survival (RFS) (HR 0.74, \( P = .029 \)) as compared with ASCT. They concluded that alloHSCT is to be preferred over chemotherapy as Post Remission Treatment in patients with intermediate and poor-risk AML aged 40-60 years, whereas ASCT remains a treatment option to be considered in patients with intermediate-risk AML.

The importance of Minimal Residual Disease at time of transplant was also demonstrated by the same group: the HOVON/SAKK AML 42A study,\(^1 \) showed that high MRD values > 0.1% of the white blood cell count, evaluated by immunophenotyping, were associated with a higher risk of relapse in patients with either good- or intermediate-risk cytogenetic markers. In this study for the 54 patients with undetectable MRD who were consolidated with ASCT, the 4-year relapse incidence was 33%, and the LFS 63%.

Messina et al. evaluated the MRD marker Wilms’ tumor gene 1 (WT1) by real-time PCR in 30 consecutive patients autografted for AML.\(^{14} \) All patients showed WT1 overexpression at the time of diagnosis and were in morphological and genetic CR at the time of leukapheresis. A cut-off value of 80 WT1 copies/10^6 ABL copies was used to differentiate MRD-positive and MRD-negative leukapheresis products. Relapse incidence was 87% for patients transplanted with MRD-positive leukapheresis but only 30% for those transplanted with MRD-negative leukapheresis products \( (P = .0001) \), indicating the usefulness of WT1 as a marker of MRD to predict relapse after ASCT and determine the optimal consolidation strategy.

In a study on the impact of the pretransplant regimen prior to ASCT,\(^{16} \) we recently compared the association of Busulfan and high

### TABLE 2 | Multivariate analysis of prognostic factors in the ELN intermediate 1 genetic group

<table>
<thead>
<tr>
<th>Intermediate I</th>
<th>RI</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
<th>NRM</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
<th>LFS</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
<th>OS</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>UD 10/10 vs. Auto</td>
<td>0.24</td>
<td>0.14-0.39</td>
<td>.&lt;10^-5</td>
<td>2.45</td>
<td>0.67-9</td>
<td>.18</td>
<td>0.36</td>
<td>0.24-0.56</td>
<td>&lt;10^-5</td>
<td>0.53</td>
<td>0.33-0.85</td>
<td>.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>0.81</td>
<td>0.68-0.96</td>
<td>.016</td>
<td>1.24</td>
<td>0.83-1.85</td>
<td>.29</td>
<td>0.88</td>
<td>0.75-1.03</td>
<td>.11</td>
<td>1</td>
<td>0.84-1.19</td>
<td>.99</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year of Transplant</td>
<td>1.01</td>
<td>0.92-1.11</td>
<td>.78</td>
<td>1.09</td>
<td>0.9-1.32</td>
<td>.40</td>
<td>1.03</td>
<td>0.95-1.12</td>
<td>.47</td>
<td>1.04</td>
<td>0.95-1.14</td>
<td>.41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time diag-T (mo)</td>
<td>1</td>
<td>0.93-1.09</td>
<td>.84</td>
<td>0.9</td>
<td>0.7-1.15</td>
<td>.38</td>
<td>0.99</td>
<td>0.91-1.07</td>
<td>.73</td>
<td>0.97</td>
<td>0.87-1.07</td>
<td>.51</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PB vs. BM</td>
<td>1.82</td>
<td>0.85-3.89</td>
<td>.13</td>
<td>0.75</td>
<td>0.26-2.17</td>
<td>.6</td>
<td>1.41</td>
<td>0.77-2.6</td>
<td>.27</td>
<td>1.22</td>
<td>0.63-2.37</td>
<td>.56</td>
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</tbody>
</table>

UD transplants are associated with lower RI, better LFS and OS.

### TABLE 3 | Multivariate analysis of prognostic factors in the ELN intermediate 2 genetic group

<table>
<thead>
<tr>
<th>Intermediate II</th>
<th>RI</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
<th>NRM</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
<th>LFS</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
<th>OS</th>
<th>HR</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>UD 10/10 vs. Auto</td>
<td>0.71</td>
<td>0.36-1.42</td>
<td>.33</td>
<td>6.12</td>
<td>1.18-31.66</td>
<td>.03</td>
<td>1.09</td>
<td>0.59-2</td>
<td>.79</td>
<td>1.15</td>
<td>0.57-2.29</td>
<td>.70</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.17</td>
<td>0.91-1.5</td>
<td>.23</td>
<td>1.64</td>
<td>0.96-2.81</td>
<td>.073</td>
<td>1.26</td>
<td>1.01-1.58</td>
<td>.04</td>
<td>1.45</td>
<td>1.10-1.91</td>
<td>.008</td>
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<td></td>
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</tr>
<tr>
<td>Year of Transplant</td>
<td>1.05</td>
<td>0.91-1.2</td>
<td>.51</td>
<td>0.8</td>
<td>0.61-1.04</td>
<td>.1</td>
<td>0.98</td>
<td>0.87-1.11</td>
<td>.73</td>
<td>0.98</td>
<td>0.86-1.13</td>
<td>.81</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Time diag-T (mo)</td>
<td>0.97</td>
<td>0.83-1.13</td>
<td>.69</td>
<td>1.4</td>
<td>1.12-1.75</td>
<td>.003</td>
<td>1.07</td>
<td>0.95-1.21</td>
<td>.27</td>
<td>1.05</td>
<td>0.91-1.22</td>
<td>.49</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PB vs. BM</td>
<td>1.33</td>
<td>0.45-3.93</td>
<td>.61</td>
<td>0.67</td>
<td>0.13-3.49</td>
<td>.64</td>
<td>1.11</td>
<td>0.46-2.7</td>
<td>.82</td>
<td>0.84</td>
<td>0.31-2.26</td>
<td>.73</td>
<td></td>
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</table>

NRM higher with UD. No difference in LFS and OS with ASCT or UD transplants.
dose Melphalan (BUMEL) with the historical association of Busulfan and Cyclophosphamide (BUCY): we found that BUMEL was associated with a significantly lower R1 and better LFS; in addition, more relevant to the present study, we also found in the 74 BUMEL and 187 BUCY patients known to be autografted in molecular remission, a high LFS of 66% in the BUMEL group, higher than the 47% observed in the BUCY group. All these studies support the assumption that high dose consolidation with ASCT may bring more benefit to chemosensitive AML patients, especially those in molecular CR. This would be in line with the first report, already thirty years ago, which showed that the benefit of ASCT for diffuse large cell lymphomas in relapse was in fact restricted to chemosensitive patients, leading to the historic concept of ASCT being used to serve as a "hammer to kill a fly", where the "fly" represented MRD.

In the present study all patients included had cytogenetics available and were reported as in first molecular remission at time of transplantation. To compare the outcomes following ASCT and matched UD transplants, we decided to stratify the patients using the proposed European Leukemia Net (ELN) standardized reporting for correlation of cytogenetic and molecular genetic data in AML with clinical data published in 2010.19 Using this approach in a series of 1550 adult patients treated on first line trials which did not include allogeneic stem cell transplantation in first CR, the Cancer and Leukemia Group B18 reported, in patients below 60 years of age, LFS and OS at 3 years of 55% and 66% in the favorable group, 23% and 28% in the intermediate risk 1 group and 34% and 45% in the intermediate risk 2 group. For patients autografted in the present EBMT study, the LFS and OS at two years of 67% and 83% in the good risk, 39% and 60% in the intermediate risk 1 and 60% and 74% in the intermediate risk 2 group at 2 years follow the same correlation. Worse outcome in the intermediate 1 risk group can be explained by the inclusion in this category of all AML with the FLT3ITD abnormality which has been since 2005 one of the strongest recognized negative prognostic factor.24,25 Interestingly, matched UD transplants somehow erased the ELN prognostic classification with outcomes that remained equivalent in the three groups, ie LFS and OS of 62% and 64% in the favorable group, 70% and 74% in intermediate 1 and 64% and 71% in intermediate 2 group. When considering the nature of the high dose consolidation to apply to adult patients with AML in first molecular remission, using the ELN prognostic classification, this study shows that while the outcome of UD transplants does not differ within groups, the outcome post ASCT varies: good risk patients have a better outcome with ASCT than with UD transplants. Patients in the intermediate risk 2 category have the same outcome post ASCT or UD transplants and in this category, one may argue that the absence of GVHD and the better quality of life post transplant may favor ASCT. Finally, patients in the intermediate risk 1 category do better with UD transplants.

This study is a retrospective cohort study with its inherent limitations. To avoid selection bias of specific subpopulations in one of the 2 groups compared, we selected all consecutive patients fitting the inclusion criteria, whatever the associated treatment, to mimic an intent-to-treat analysis. Consequently, there was some heterogeneity in the conditioning regimens utilized in both the autografted population who received a myeloablative conditioning regimen as well as in recipients of adult unrelated donor transplants who for half of them received a myeloablative conditioning regimen and for the other half a reduced intensity conditioning regimen. However most of these conditioning regimens when used were considered as standard. Nonetheless one may also argue that there has been over the time of this study some reduction in NRM following allo transplantation leading to results of current practice more favorable for UD allotransplants. We however did not see any improvement in outcome both for autologous and allo geneic transplants in patients transplanted before or after 2012, median year of transplantation. Such a retrospective study cannot totally avoid confounding by indication, the individual characteristics of a patient being the primary confounders. This would be prevented completely only with a randomized clinical trial. We have no in-depth information on the reason why a patient was in the end autografted or allografted, aside from the fact that they all were in molecular remission when the decision was taken. In addition, treatment policy differed among centers, some centers offering the possibility of an autograft while other considered unrelated donor transplants as a priority option in the absence of an identical sibling donor. However, interestingly, there was no imbalance among centres doing autologous transplantation only (85 centres reporting 259 patients) and centres doing allogeneic transplantation only (63 centres reporting 228 patients). Even in the 28 centres doing both autologous and allogeneic transplantation, the numbers of patients autografted (114) and allografted (107) were similar. We checked for a centre effect which we did not find. Finally, the status of molecular remission was defined locally by each center, in relation with the molecular marker identified and the thresholds of detection retained by each center. We recognize that the thresholds for the definition of molecular remission have diminished over time. However, whatever the thresholds considered, patients in molecular CR in all studies published so far had a better prognosis. While an up to date confirmation of the status of molecular CR in a centralized facility would have been the rule in a prospective randomized study, this golden standard was impossible to apply to this retrospective analysis. Despite these reservations, we believe the data here presented raise an important issue in a selected population of chemosensitive patients who may get benefit from autografting resulting in a potentially long term better quality of life. Our study may justify reconsidering randomized studies including ASCT in AML patients in molecular remission.

In the past five years or so, new tools have been developed for the control of AML MRD and relapse prevention. For instance sorafenib has been recently introduced as maintenance therapy post allogeneic transplantation. We unfortunately do not have information on the use of sorafenib in the present EBMT registry.

However if sorafenib improves the outcome post transplantation, it would concern specifically patients in the intermediate risk 1 genetic group with the FLT3-ITD. In this group we already found that UD transplants were associated with a better LFS and OS than autologous transplants.

EBMT is presently launching a specific study on the impact of sorafenib in patients with AML and the FLT3-ITD marker, who received sorafenib post allogeneic transplant.

Other recent tools are targeted therapies including monoclonal antibodies and CART cells.26 ASCT may well become an ideal platform
for immunotherapy post transplant. Adult patients with AML in the favorable and intermediate 2 genetic risk groups in mCR1 may in the near future get benefit from ASCT followed by immunotherapy, avoiding the risk of developing extensive chronic graft versus host disease.

CONFLICT OF INTERESTS
No conflict of interest disclaimed.

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SUPPORTING INFORMATION
Additional Supporting Information may be found online in the supporting information tab for this article.