Intermediate-Dose versus Low-Dose Cyclophosphamide and Granulocyte Colony-Stimulating Factor for Peripheral Blood Stem Cell Mobilization in Patients with Multiple Myeloma Treated with Novel Induction Therapies

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Peripheral blood progenitor cell mobilization with intermediate-dose cyclophosphamide (ID-CY) and granulocyte colony-stimulating factor (G-CSF) has been shown to be more efficacious, albeit more toxic, than low-dose cyclophosphamide (LD-CY) mobilization regimens in patients with multiple myeloma treated with conventional therapies. However, the relative importance of cyclophosphamide dose intensity in peripheral blood progenitor cell mobilization after novel induction regimens is not known. Here we report mobilization outcomes of 123 patients who underwent transplantation within 1 year of starting induction chemotherapy with novel agents. We compared consecutive patients undergoing mobilization with ID-CY/G-CSF (3–4 g/m²) at one institution (n = 55) with patients receiving LD-CY/G-CSF (1.5 g/m²) at a different transplantation center (n = 68). At baseline, the 2 groups were well balanced, except for more frequent previous lenalidomide use in the ID-CY group (P = .04). Compared with LD-CY, ID-CY use was associated with higher median peak PB CD34+ cell count (35/μL versus 160/μL; P < .001), CD34+ cell yield on day 1 of collection (2.6 × 10⁶/kg versus 11.7 × 10⁶/kg, P ≤ .001), and total CD34+ cell yield (7.5 × 10⁶/kg versus 16.6 × 10⁶/kg, P ≤ .001). Six patients in the LD-CY group had mobilization failure, compared with no patients in the ID-CY group. A significantly higher proportion of patients in the LD-CY group (P < .001) were unable to collect ≥ 5 × 10⁶/kg and ≥ 10 × 10⁶/kg CD34+ cells. Neutrophil and platelet engraftment were significantly faster in the ID-CY group, likely because of higher infused CD34+ cell doses. In conclusion, compared with LD-CY, ID-CY produced a more robust peripheral blood progenitor cell mobilization and significantly reduced the rates of mobilization failure. These data caution against the use of LD-CY–containing mobilization strategies in patients with multiple myeloma undergoing stem cell collection after novel induction regimens.


KEY WORDS: Chemomobilization, Autologous transplantation, Lenalidomide, High dose therapy
CD34$^+$ cells/kg when mobilized with G-CSF alone [6-8]. In contrast, mobilization with chemotherapy (mostly cyclophosphamide) in addition to G-CSF has been shown to improve PBPC collection yield and reduce mobilization failure rates compared with G-CSF alone [9]. Limited retrospective data suggest that cyclophosphamide may overcome the effects of previous lenalidomide exposure on PBPC mobilization in patients with MM [10].

The cyclophosphamide doses used for mobilization of PBPCs in patients with MM have ranged from 1 g/m$^2$ up to 7 g/m$^2$ in previous studies. Several studies have assessed the relative impact of cyclophosphamide dose intensity on PBPC mobilization in patients with MM treated with conventional chemotherapy regimens [11-14]. In general, PBPC mobilization with high-dose cyclophosphamide (HD-CY; 7 g/m$^2$) plus G-CSF was found to be significantly more toxic compared with intermediate-dose cyclophosphamide (ID-CY; 3–4 g/m$^2$) and G-CSF, with no convincing evidence of superior efficacy [11,15]. Studies comparing mobilization with ID-CY plus G-CSF with low-dose cyclophosphamide (LD-CY; 1-2 g/m$^2$) plus G-CSF reported higher total CD34$^+$ cell yield with ID-CY, but at the cost of higher toxicity. However, no significant difference in mobilization failure rates between ID-CY and LD-CY mobilization has been reported [13,14]. Whether the lack of a clear difference in efficacy between ID-CY and LD-CY in patients with MM receiving conventional induction regimens still holds in the era of novel induction therapies is not known. Determining the cyclophosphamide dose with the best risk/benefit ratio for PBPC mobilization is critical to assessing the efficacy of novel mobilization regimens against chemotherapy-based mobilizing strategies. Here we report our retrospective data comparing the efficacy and toxicity of PBPC mobilization with G-CSF and either ID-CY or LD-CY in patients with MM receiving novel induction regimens.

**PATIENTS AND METHODS**

**Patient Population**

A total of 123 consecutive adult patients with MM undergoing HDT and autologous peripheral blood HCT after PBPC mobilization with cyclophosphamide plus G-CSF at Georgia Health Sciences University (GHSU) or West Virginia University Hospitals (WVUH) were included in this study. All patients underwent a planned, single autologous transplantation within 1 year of starting an induction chemotherapy regimen containing at least one novel agent (ie, thalidomide, lenalidomide, or bortezomib) between January 2003 and February 2011. Patients meeting these criteria and undergoing mobilization with cyclophosphamide 1.5 g/m$^2$ and G-CSF constituted the LD-CY group, and those receiving cyclophosphamide 3-4 g/m$^2$ and G-CSF during the same period formed the ID-CY group. The study was approved by the Institutional Review Board and Protocol Review and Monitoring Committee at GHSU and WVUH.

**PBPC Mobilization and Collection**

ID-CY was used for PBPC mobilization at GHSU. Cyclophosphamide was administered as a 3-hour i.v. infusion at a dose of 1.5 g/m$^2$/day in 11 patients and 2 g/m$^2$/day in 44 patients on days 1 and 2, along with MESNA. All patients received antiemetic prophylaxis with ondansetron 20 mg i.v. 30 minutes before chemotherapy and hydration with 1,000 mL of normal saline before chemotherapy. G-CSF (10 μg/kg/day subcutaneously) was started on day +3 and continued until the completion of apheresis. All patients in the ID-CY arm received antimicrobial prophylaxis with levofloxacin, acyclovir, and fluconazole. At WVUH, LD-CY was used for PBPC mobilization during the study period, as described previously [16,17]. In brief, cyclophosphamide was administered at a uniform dose of 1.5 g/m$^2$ i.v. over 2 hours on day 1. All patients received antiemetic prophylaxis with ondansetron 24 mg orally 1 hour before chemotherapy, along with hydration with 500 mL of normal saline before and after chemotherapy. G-CSF (10 μg/kg/day s.c.) was started on day +8 and continued until the completion of apheresis. No antimicrobial prophylaxis was used in the LD-CY group.

Peripheral blood CD34$^+$ cell count was measured daily when patients’ white blood cell count recovered to ≥4,000/μL or from day +12 onward (whichever occurred first). When the peripheral blood CD34$^+$ cell count was ≥10/μL, apheresis was started. All collections were performed with a COBE Spectra Apheresis System (CaridianBCT, Lakewood, CO), processing 3 to 4 blood volumes. It is the institutional policy at both transplantation centers to routinely target collection of a sufficient number of CD34$^+$ cells (ie, a minimum of 5 × 10$^6$ CD34$^+$ cells/kg and a target of ≥10 × 10$^6$ CD34$^+$ cells/kg) to administer 2 rounds of HDT and autologous HCT. (None of the patients at either transplantation center underwent a planned tandem autograft, however.) Measurements of peripheral blood CD34$^+$ cell count and CD34$^+$ cell content of the apheresis product were performed at the GHSU HLA Laboratory and the WVUH Flow Cytometry Laboratory. A FACSCanto II flow cytometer (BD Biosciences, Sparks, MD) was used for all analyses. Lysed and washed RBC samples were used for CD34$^+$ cell enumeration with PE-labeled, 8G12 clone immunoglobulin G1 (BD Biosciences) based on International Society of Hematotherapy and Graft Engineering guidelines [18]. The final products were cyropreserved.
in 10% DMSO using a controlled-rate freezer and stored in liquid nitrogen.

**Transplantation Procedure and Supportive Care**

All patients received uniform conditioning with melphalan 200 mg/m² (reduced to 140 mg/m² in patients with renal insufficiency) on day -2, followed by infusion of autologous PBPCs on day 0. All patients received posttransplantation growth factor support (G-CSF 5 μg/kg), along with fungal (fluconazole), herpes zoster/herpes simplex (acyclovir or valacyclovir), and bacterial prophylaxis (ciprofloxacin or levofloxacin) in accordance with institutional guidelines. The time of neutrophil engraftment was considered the first of 3 consecutive days with an absolute neutrophil count ≥0.5 × 10⁹/L after a posttransplantation nadir. The time of platelet engraftment was considered the first of 3 consecutive days with a platelet count ≥20 × 10⁹/L, in the absence of platelet transfusion in the preceding 7 days.

**Statistical Analysis**

Baseline categorical variables were compared using the χ² test, and continuous variables were compared using the Wilcoxon rank-sum test or 2-sample t-test as appropriate. Successful mobilization was defined as a total of ≥2 × 10⁹ CD34⁺ cells/kg patient body weight in the final product. “Good mobilizers” were defined as patients collecting ≥5 × 10⁶ CD34⁺ cells/kg in 1-2 days, as described previously [4]. To account for differences in the number of collection days across patients, data on peak peripheral blood CD34⁺ collection on day 1 of apheresis only were analyzed. Nonrelapse mortality (NRM) was defined as any death without evidence of disease relapse or progression. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method. OS was defined as the time from transplantation to death from any cause, and surviving patients were censored at last follow-up. PFS from transplantation was calculated using death and disease progression and/or relapse as events. OS and PFS data were analyzed using the log-rank test. All P values were 2-sided. Variables associated with OS and PFS analyses were run using Cox proportional hazard regression. Variables that demonstrated an association (P ≤ .10) were then entered into a multivariate analysis. Analyses were performed using SPSS 13 (SPSS Inc, Chicago, IL).

**RESULTS**

**Patient Characteristics**

The baseline characteristics of the 123 consecutive patients included in this analysis are presented in Table 1. Sixty-eight patients underwent mobilization with LD-CY, and the other 55 patients received ID-CY. The 2 groups did not differ significantly in terms of patient age, sex, Durie-Salmon stage at diagnosis, cytogenetic risk, number of previous therapies, overall bone marrow cellularity before transplantation, degree of bone marrow involvement with clonal plasma cells, and remission status before transplantation. The median Karnofsky performance score (KPS) was significantly higher in the LD-CY group, however; there was no difference in the baseline Hematopoietic Cell Transplantation Comorbidity Index between the 2 groups. Previous radiotherapy was more frequent in the ID-CY group (18.1% versus 32.2%); however, this difference was not statistically significant. The ID-CY group also had a higher proportion of African-American patients, as well as more frequent lenalidomide exposure before mobilization (40% versus 22%; P = .04).

**Efficacy Characteristics**

The patients in the LD-CY group started apheresis at a mean of 12.06 days (median, 12 days; range, 11-14 days) after cyclophosphamide administration, compared with a mean of 12.61 days (median, 12 days; range, 11-15 days; P < .001) in the ID-CY group. The total CD34⁺ cell yield was significantly higher in the ID-CY group (median collection, 16.6 × 10⁹ cells/kg versus 7.5 × 10⁶ cells/kg; P < .001) (Table 2). To account for differences in the number of collection days across patients, we compared peak peripheral blood CD34⁺ cell count and CD34⁺ cell collection on day 1 of apheresis only. Mobilization with LD-CY was associated with significantly higher peak peripheral blood CD34⁺ cell count (P < .0001) and day 1 CD34⁺ cell count (P < .001). PBPC mobilization failure was significantly more common in the LD-CY group (8.8% versus 0%; P = .03). As detailed in Table 2, ID-CY was significantly superior to LD-CY in the majority of the mobilization efficacy parameters analyzed, including the number of patients collecting ≥2 million CD34⁺ cells/kg on day 1, number of patients collecting a total of ≥5 and ≥10 million CD34⁺ cells/kg, and the proportion of patients requiring more than 2 apheresis sessions. There was no significant difference between the 2 groups in terms of total number of apheresis sessions and the number of patients meeting the definition of a good mobilizer as defined by Wood et al [4].

We next assessed the efficacy of mobilization in the subgroup of patients who received lenalidomide before transplantation. Fifteen patients in the LD-CY group and 22 patients in the ID-CY group had received a previous lenalidomide-based regimen (P = .04). Three patients (20%) in the LD-CY group with previous lenalidomide treatment experienced mobilization failure, compared with none in the ID-CY group.
Similarly, a significantly higher proportion of lenalidomide-treated patients in the ID-CY group were able to collect $5 \text{ million CD34}^+ \text{ cells/kg (100\% versus 73.3\%; } P = .02\text{)}$ and $10 \text{ million CD34}^+ \text{ cells/kg (77.2\% versus 26.6\%; } P = .006\text{)},$ and significantly fewer patients in the ID-CY group required more than 2 apheresis sessions ($22.7\% \text{ versus 73.3\%; } P = .006\text{). All patients who failed PBPC mobilization with ID-CY subsequently underwent successful bone marrow harvest or remobilization with AMD3100/G-CSF.

**Toxicity and Supportive Care**

Four patients (5.8\%) in the LD-CY group and 9 patients (16.3\%) in the ID-CY group experienced an episode of febrile neutropenia ($P = .08\text{)}$ (Table 3). There was no significant difference between the 2 groups in the use of i.v. antibiotics (7.3\% versus 16.3\%; $P = .11\text{). Hospitalization was required in 10.2\% of the patients in the LD-CY group, compared with 20\% of patients in the ID-CY group ($P = .20\text{). There was a trend toward longer hospital stays in the ID-CY group (median, 4 days versus 3 days; } P = .07\text{). Compared with the LD-CY group, significantly more patients in the ID-CY group required packed RBC (8.8\% versus 34.5\%; } P = .001\text{) and platelet transfusions (2.9\% versus 21.8\%; } P = .003\text{) between day 1 of cyclophosphamide administration and completion (or termination) of PBPC collection. There were no mobilization-related deaths or intensive care unit admissions in either group.
3-year NRM rates were 1.8% (n = 5) significantly associated with OS. The day-100 NRM was 40% for the ID-CY group (17 days [range, 8-40 days] versus 14 days [range, 8-15 days]; P < .001). The median time to neutrophil engraftment was significantly shorter in the ID-CY group (10 days [range, 9-53 days] versus 14 days [range, 11-35 days]; P < .001). Similarly, the median time to platelet engraftment was significantly shorter in the ID-CY group (17 days [range, 8-40 days] versus 18 days [range, 9-53 days]; P = .02). The median follow-up of the surviving patients was 29.5 months. The 3-year PFS was 44% for the LD-CY group and 40% for the ID-CY group (P = .62). The 3-year OS was significantly better in the ID-CY group (84% versus 68%; P = .008) (Figure 1). On multivariate analysis, KPS (hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.87-0.99; P = .02), infused CD34+ cell dose (HR, 0.72; 95% CI, 0.53-0.97; P = .03), and cyclophosphamide dose (HR, 18.2; 95% CI, 1.5-212.7; P = .02), were variables significantly associated with OS. The day-100 NRM was 1.8% (n = 1) for the ID-CY group and 2.9% (n = 2) for the LD-CY group (P = .68), and the corresponding 3-year NRM rates were 1.8% (n = 1) and 10.2% (n = 7) (P = .058). The causes of NRM in the LD-CY group included gram-negative sepsis before day 100 (n = 1), pneumonia before day 100 (n = 1), cerebrovascular accident (n = 2), heart disease (n = 1), second malignancy (n = 1), and unknown (n = 1). The cause of NRM in the ID-CY group was sepsis before day +100.

**DISCUSSION**

In this study, we analyzed the relative importance of cyclophosphamide dose intensity on PBPC mobilization outcome in patients with MM undergoing autologous HCT after novel induction therapies and found several interesting results. First, our data suggest that a higher cyclophosphamide dose is associated with a lower rate of PBPC mobilization failure. Second, with higher cyclophosphamide dose, significantly more patients are able to collect a sufficient number of CD34+ cells to potentially undergo 2 rounds of HDT. Third, it appears that this higher dose, while requiring more transfusion support, was not clearly associated with significant increases in hospitalization and the need for i.v. antibiotics.

The cyclophosphamide doses used for PBPC mobilization in patients with MM varied widely (range, 1-7 g/m²) in previous studies. Compared with ID-CY plus G-CSF, HD-CY for PBPC mobilization in patients with MM treated with conventional chemotherapy regimens is significantly more toxic, without convincing evidence of superior efficacy [11,15]. Previous studies comparing ID-CY plus G-CSF and LD-CY plus G-CSF have reported higher total CD34+ cell yield with ID-CY, but at the cost of higher toxicity [13,14]. Whether the lack of a clear difference in efficacy between ID-CY and LD-CY in patients with MM treated with conventional chemotherapy regimens remains true in the era of novel agents is unknown.

In previous retrospective studies of patients with MM treated with conventional chemotherapy regimens (mostly combinations of vincristine, adriamycin, and dexamethasone), PBPC mobilization with ID-CY plus G-CSF produced higher peak peripheral blood CD34+ cell counts [14] and higher total CD34+ cell yield [13,14] compared with LD-CY plus G-CSF, but with no difference in the rate of mobilization failure as defined in our study. In contrast, we report here (in the largest study to date, to our knowledge) that in the era of novel therapies, LD-CY-based mobilization is associated with a significantly higher rate of stem cell mobilization failure. This is especially noteworthy, because the 2 groups in our study were closely matched for parameters that can potentially affect PBPC mobilization.

### Table 2. Mobilization Outcomes According to Cyclophosphamide Dose

<table>
<thead>
<tr>
<th></th>
<th>LD-CY (n = 68)</th>
<th>ID-CY (n = 55)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Peak peripheral CD34+ cell count, µL, mean/median (range)</td>
<td>56.8/35 (6-309)</td>
<td>255.4/160 (19-1961)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CD34+ cells × 10⁶/kg collected on day 1, mean/median (range)</td>
<td>4.05/2.6 (0-15)</td>
<td>16/11.7 (0-61)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total CD34+ cells × 10⁶/kg collected, mean/median (range)</td>
<td>7.8/7.5 (0-18)</td>
<td>24.9/16.6 (2-82)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total number of apheresis sessions, mean/median (range)</td>
<td>2.49/2 (1-5)</td>
<td>2.2/2 (1-6)</td>
<td>.25</td>
</tr>
<tr>
<td>Mobilization failures, n (%)</td>
<td>6 (8.8)</td>
<td>0 (0)</td>
<td>.03</td>
</tr>
<tr>
<td>Patients collecting ≥2 × 10⁶ CD34+ cells/kg on day 1, n (%)</td>
<td>41 (60.3)</td>
<td>48 (87.3)</td>
<td>.001</td>
</tr>
<tr>
<td>Patients collecting ≥5 × 10⁶ CD34+ cells/kg, n (%)</td>
<td>47 (69.1)</td>
<td>53 (96.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Patients requiring more than 1 apheresis session, n (%)</td>
<td>56 (82.3)</td>
<td>53 (96.4)</td>
<td>.02</td>
</tr>
<tr>
<td>Patients requiring more than 2 apheresis sessions, n (%)</td>
<td>30 (44.1)</td>
<td>12 (21.8)</td>
<td>.01</td>
</tr>
<tr>
<td>Good mobilizers, n (%)</td>
<td>30 (63.8)</td>
<td>42 (79.2)</td>
<td>.12</td>
</tr>
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</table>

Note: *Mobilization failure is defined as a total CD34+ cell yield of <2 × 10⁶ cells/kg.

*Good mobilizers are defined as patients collecting ≥5 × 10⁶ CD34+ cells/kg in ≤2 days.
mobilization, including patient age, stage, previous therapy, number of lines of previous therapy, time between diagnosis and transplantation, pretransplantation bone marrow cellularity, and degree of bone marrow plasmacytosis, except for a significantly higher previous lenalidomide exposure in the ID-CY group. In line with conventional chemotherapy-era data, in the present study, ID-CY produced higher peak peripheral blood CD34<sup>+</sup> cell counts and a significantly higher total CD34<sup>+</sup> cell yield. More importantly, a significantly higher proportion of ID-CY patients were able to meet our institutional goals of minimum (≥5 million CD34<sup>+</sup> cells/kg) and target (≥10 million CD34<sup>+</sup> cells/kg) CD34<sup>+</sup> cell yield without the need for a greater number of apheresis sessions. Although we acknowledge that optimal CD34<sup>+</sup> collection yield (and thus the optimal collection target) is controversial, similar minimum and target levels with slight variations have been used by other investigators [4,19,20] and international myeloma working group guidelines [5,21].

The significantly higher requirements for packed RBC and platelet transfusion support in our ID-CY group is in agreement with the majority of previous studies using similar doses of cyclophosphamide [13,19,22]. However, unlike previous studies in which ID-CY was associated with significantly higher rates of febrile neutropenia, i.v. antibiotic use, and need for hospitalization [13,14,19] compared with LD-CY, these rates were not significantly higher in our ID-CY group, with only a trend toward longer hospitalization seen in this group (P = .07). It is possible that our analysis was not sufficiently powered to detect a difference in infectious complications, however. In contrast to previous studies, our ID-CY patients were routinely given prophylactic antibiotics, which might have reduced the rates of febrile neutropenia and subsequent need for i.v. antibiotics and hospitalization.

Previous therapy with lenalidomide is known to negatively affect PBPC mobilization [7,8]. In a study of 28 patients with MM treated with a combination of dexamethasone, clarithromycin, and lenalidomide, Mark et al [10] reported sufficient stem cell collection for 2 autologous HCTs from all patients mobilized with cyclophosphamide (3 g/m<sup>2</sup>) plus G-CSF versus adequate collection in only 33% of patients mobilized with G-CSF alone. This finding suggests that this approach can potentially overcome the impaired PBPC mobilization associated with lenalidomide [5]. Our study provides further data indicating that although ID-CY plus G-CSF can potentially overcome lenalidomide-related impairment of PBPC mobilization, this effect is probably dose-related, and LD-CY-containing regimens remain associated with a high risk of mobilization failure and a significantly lower stem cell yield.

DiPersio et al [23] in a phase III study, found that AMD3100 (plerixafor) plus G-CSF was significantly superior to G-CSF plus placebo for PBPC mobilization in patients with MM. To the best of our knowledge, no prospective trials comparing AMD3100 plus G-CSF and cyclophosphamide plus G-CSF have been published to date. Determining the cyclophosphamide dose with the best risk/benefit ratio for PBPC mobilization is critical for prospectively

### Table 3. Toxicity and Supportive Care

<table>
<thead>
<tr>
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<th>LD-CY (n = 68)</th>
<th>ID-CY (n = 55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenic fever, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4 (5.8)</td>
<td>9 (16.3)</td>
<td>.08</td>
</tr>
<tr>
<td>Need for i.v. antibiotics, n (%)</td>
<td>5 (7.3)</td>
<td>9 (16.3)</td>
<td>.11</td>
</tr>
<tr>
<td>Packed RBC transfusion, n (%)</td>
<td>6 (8.8)</td>
<td>19 (34.5)</td>
<td>.001</td>
</tr>
<tr>
<td>Platelet transfusion, n (%)</td>
<td>2 (2.9)</td>
<td>12 (21.8)</td>
<td>.003</td>
</tr>
<tr>
<td>Hospitalization, n (%)</td>
<td>7 (10.2)</td>
<td>11 (20)</td>
<td>.20</td>
</tr>
<tr>
<td>Days of hospitalization, mean/median (range)</td>
<td>6/3 (1-5)</td>
<td>11/4 (1-9)</td>
<td>.07</td>
</tr>
</tbody>
</table>

<sup>a</sup>A single episode of fever of ≥101.4°F or 2 episodes of fever >100.4°F at least 1 hour apart in a patient with an absolute neutrophil count of <500/μL.

![Figure 1](image-url). Kaplan-Meier curves of PFS (A) and OS (B) relative to cyclophosphamide dose intensity. The solid curve represents LD-CY; the dashed curve, ID-CY.
assessing the efficacy of novel AMD3100-based mobilization regimens against an optimally dosed chemotherapy-based mobilizing strategy. Shaughnessy et al [19] retrospectively compared mobilization with AMD3100 plus G-CSF with cyclophosphamide (3-5 g/m²)-based chemomobilization. There was no significant difference between the 2 groups of patients in terms of total CD34⁺ cells collected, mobilization costs, and clinical outcomes. Cyclophosphamide mobilization was associated with higher rates of hospitalization, however. Comparison of these mobilization strategies merits prospective investigations.

A surprising finding of the present study is the superior OS of the ID-CY group. As far as we know, no previous studies have reported a survival benefit attributable to PBPC mobilization strategy (except for the known benefit of peripheral blood autografts over bone marrow autografts). Although cyclophosphamide has activity against MM, we caution against overinterpreting the OS benefit seen in the ID-CY group in this retrospective study. It is possible that this benefit is due largely to the significantly higher CD34⁺ cell dose infused in these patients, with resulting faster neutrophil engraftment and reduced infectious complications. Improved survival outcomes in patients with MM receiving a higher infused CD34⁺ cell dose have been reported by others as well [24]. Although we noted a trend toward a higher 3-year NRM in our LD-CY group, the majority of these patients did not die due to infectious complications. It is also possible that differences in posttransplantation maintenance strategies, imbalances in access to investigational therapies, or unknown biological differences might contribute to this survival difference in our 2 groups.

In conclusion, the present study found robust mobilization of PBPCs in patients with MM treated with novel agents, including the challenging subgroup of lenalidomide-treated patients, with an ID-CY plus G-CSF regimen, with no significant increase in infectious complications or morbidity. Our data caution against the use of LD-CY-containing mobilization regimens in patients with MM receiving induction therapy with novel agents.

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