Gemcitabine, dexamethasone and cisplatin (GDP) is an effective and well-tolerated mobilization regimen for relapsed and refractory lymphoma: a single center experience

Hikmetullah BATGI1, Semih BAŞCI1*, Mehmet Sinan DAL1, Merih KIZIL ÇAKAR1, Bahar UNCU ULU1, Tuğçe Nur YİĞENOĞLU1, Nurgül ÖZCAN1, Ali KILINÇ2, Alparslan MERDİN1, Jale YILDIZ1, Mehmet BAKIRTAŞ1, Derya ŞAHİN1, Tahir DARÇIN1, Dicle İSKENDER1, Nuran Ahu BAYSAL1, Fevzi ALTUNTAŞ1

1Department of Hematology and Bone Marrow Transplantation Center, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, University of Health Sciences, Ankara, Turkey
2Department of Clinical Biochemistry, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, University of Health Sciences, Ankara, Turkey

Background/aim: Gemcitabine, dexamethasone and cisplatin (GDP) is a well-established salvage regimen for relapsed and refractory lymphomas. In this study, we aimed to share our experience with the patients who received GDP/R-GDP (rituximab-gemcitabine, dexamethasone and cisplatin) for stem cell mobilization.

Materials and methods: Data of 69 relapsed and refractory Hodgkin lymphoma (HL) and Non-Hodgkin lymphoma (NHL) patients who received GDP/R-GDP as salvage chemotherapy in our center between July 2014 and January 2020 were retrospectively evaluated. After the evaluation of response, 52 patients had a chemosensitive disease and underwent mobilization with GDP/R-GDP plus G–CSF (granulocyte colony-stimulating factor). Collected CD34+ stem cells and related parameters were compared in terms of diagnosis of HL and NHL, early and late stage, patients who did not receive RT and those who received RT, and patients aged under 60 and over 60.

Results: On the 15th day on average (range 11–20), a median number of $8.7 \times 10^6$ /kg (4.1–41.5) CD34+ stem cells were collected in 51 (98%) of our 52 chemosensitive patients and 1 (2%) patients failed to mobilize. We observed acceptable hematological and nonhematological toxicity. The targeted amount of $2 \times 10^6$ /kg CD34+ stem cells was attained by 98% (n: 51) patients, and all of them underwent autologous stem cell transplantation. Moreover, low toxicity profiles provide outpatient utilization option clinics with close follow-up and adequate supportive care.

Conclusion: We suggest that GDP/R-GDP plus G–CSF can be used as an effective chemotherapy regimen for mobilizing CD34+ stem cells from peripheral blood in relapsed and refractory lymphoma patients due to low toxicity, effective tumor reduction, and successful stem cell mobilization. It can also be assumed that the GDP mobilization regimen may be more effective, especially in patients with early-stage disease and in HL patients.

Key words: Gemcitabine, dexamethasone, cisplatin, stem cell mobilization, relapsed and refractory lymphoma

1. Introduction

Autologous stem cell transplantation (ASCT), which is a highly therapeutic approach to the treatment of relapsed and refractory lymphoma, is extremely dependent on the mobilization and collection of hematopoietic stem cells (HSC) [1,2]. HSCs can be collected directly from the bone marrow or peripheral blood (PB) by apheresis. ASCTs are performed primarily with peripheral blood stem cells (PBSC). The release of HSCs to PB after granulocyte colony-stimulating factor (G-CSF) treatment and/or chemotherapy is known as mobilization. CD34+ cells do not exceed 0.05% of white blood cells (WBCs) under normal conditions in PB. After combining chemotherapy and G-CSF, the number of PBSC increases from 5 to 15 times [3–5].

The target quantity of HSC to be collected is dependent on the underlying disease (Non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), and the number of transplants. The minimum dose considered to be safe in case of ASCT is $2 \times 10^6$ CD34+ cells/kg per transplant; however, the aim of many centers is higher yields of $4–5 \times 10^6$ CD34+ cells/kg as it may allow faster neutrophil and platelet (PLT) recovery, reduced hospitalization, blood transfusions, and antibiotic therapy. The ideal dose required for successful
transplantation was considered to be $5 \times 10^6$ CD34+ cells/kg [6–8]. The choice of a specific chemomobilization approach is based on the patient's disease characteristics and local clinical practice guidelines. The applications that incorporate both the G-CSF and chemotherapy regimens were shown to mobilize more PBSCs than G-CSF alone [9,10].

The combination of G-CSF and chemotherapy is favored for stem cell mobilization and for tumor burden reduction and especially those who need to harvest a greater count of stem cells. It is an option to utilize mobilization not by splitting chemotherapy apart, however, through more precise, disease definite chemotherapy regimens such as; rituximab dexamethasone cytarabine cisplatin (R-DHAP) or rituximab, ifosfamide, carboplatin, and etoposide (R-ICE) for lymphoma patients [11]. After chemotherapy regimen employment, G-CSF daily dosage for mobilization was recommended as filgrastim 10 μg/kg and lenograstim 150 μg/m². The G-CSF should be initiated following the fulfillment of chemotherapy instantly when leukocyte nadir is detected, and it should be continued till the ending of leukapheresis. Generally, it is recommended to begin G-CSF in 1–5 days following the completion of chemotherapy. Nonetheless, chemomobilization is not a panacea and has some detrimental aspects such as; therapy-associated toxicity, need for frequent hospitalization, harming bone marrow for forthcoming mobilizations and huge cost [11]. Also, it is known that repeated interventions for mobilization after failures constitute a burden for resource utilization and morbidity [12]. Considering all these factors together, determination of the most appropriate chemotherapy regimen for mobilization gains more importance [13].

The data regarding gemcitabine, dexamethasone, and cisplatin (GDP)/rituximab, gemcitabine, dexamethasone, and cisplatin (R-GDP) on stem cell mobilization are not widely investigated. This study is particularly designed to determine the results of GDP/R-GDP regimen plus G-CSF on mobilization as salvage therapy in patients with relapsed and refractory lymphoma.

2. Materials and methods

Data of 69 relapsed and refractory HL and NHL patients who received GDP/R-GDP as salvage chemotherapy in our center between July 2014 and January 2020 were retrospectively evaluated. All the patients received GDP/R-GDP as salvage regimen (rituximab 375 mg/m² on day 0, gemcitabine 1000 mg/m² on days 1 and 8, cisplatin 75 mg/m² on day 1, dexamethasone 40 mg/day on days 1, 2, 3 and 4: standard doses without dose modifications). Response assessment was based on imaging results from fluorodeoxyglucose–positron emission tomography–computed tomography (FDG/PET-CT) and computed tomography (CT) scans after treatments. The FDG/PET–CT and CT scans were evaluated by using Lugano criteria to assess FDG/PET–CT in lymphoma response criteria published in 2014 [14]. Fifty-two patients who received GDP/R-GDP had a chemosensitive disease. After GDP was given, it was the nadir for neutrophil to decrease and start to increase again, and G-CSF (2 × 5 g/kg/day) was started. Stem cell mobilization practice for lymphoma patients in our center was to start apheresis when the peripheral blood CD34+ count (PB CD34+) was > 10 cells/L, with a collection target of > $5 \times 10^6$ CD34+ cells/kg. Mobilization failure was defined as achieving a total CD34+ yield of < $2 \times 10^6$ cells/kg. Stem cell mobilization with GDP/R–GDP was compared in terms of diagnosis of HL and NHL, early and late stage, patients who did not receive RT and those who received RT, and patients under 60 and over 60 years of age.

2.1. Statistical analysis

The SPSS version 21.0 (IBM Corporation, Armonk, NY, USA) was applied to analyses. The categorical variables were presented as frequency tables, and the numerical variables were presented as either mean ± standard deviations or median and minimum–maximum values, where appropriate. Distributions of continuous variables were assessed with graphics and Kolmogorov–Smirnov test. Mann–Whitney U test was implemented to compare the nonparametric continuous variables within the groups. A chi-square test was used to analyze apheresis count frequency between the groups. A P-value ≤ 0.05 was regarded as statistically significant.

3. Results

GDP/R–GDP was given to 69 relapsed and refractory HL and NHL patients as salvage chemotherapy. Of the patients, 42 (60.9%) were males, and 27 (39.1%) were females. 38 (55%) patients had the diagnosis of HL, and 31 (45%) patients had NHL. The mean age of the patients was 43.9 ± 15.2 years. The demographic and clinical characteristics of the patients are summarized in Tables 1 and 2. After the evaluation of response to GDP or R-GDP regimen, a mobilization with G-CSF was performed for 52 patients who had a chemosensitive disease. On the 15th day, on average (range 11–20), ______ CD34+ stem cells were collected. The G-CSF mean was performed for 5 days (range 3–11). Peripheral CD34+ stem cell count before collection (on the day of collection) was between 11 and 467 cells/μL, and median number of peak CD34+ stem cells in peripheral blood was 55 cells/μL. The CD34+ stem cells were collected in 51 of our 52 chemosensitive patients (≈ 98%), and 1 (= 2%) patients failed to mobilize. In 51 patients, > $2 \times 10^6$ CD34+ stem cells/kg (median 8.68 × 10⁶, range 4.06–41.50) were successfully collected. They were collected with one leukapheresis procedure in 34 patients,
with two leukapheresis procedures in 15 patients, and with three leukapheresis procedures in 2 patients. The results of PBPCs collection are summarized in Table 3.

Demographic and clinical characteristics of the patients with successful mobilization are summarized in Table 4. The mean age of the patients with successful mobilization (n: 51) was 44 ± 14.5 years. Twenty-nine (≈ 57%) were males and 22 (≈ 43%) were females. Twenty-four (≈ 47%) patients had the diagnosis of HL, and 27 (≈ 53%) patients

Table 1. Demographic and clinical characteristics of the patients.

| Diagnosis      | HL (n: 38); NHL (n: 31) |
|---------------|-------------------------|
| Age           | 17–77 years (range) (mean age: 43.9) |
| Sex           | Male (n:42); Female (n:27) |
| Disease status| Relapse (n:40); Refractory (n:29) |
| Radiotherapy  | Yes (n:14); no. (n:55) |
| Previous number of chemo-therapies | 1 line (n: 60); 2 line (n: 7); 3 line (n: 1); 4 line (n: 1) |
| GDP/R-GDP     | GDP (n:42); R-GDP (n: 27) |
| Ann Arbor stage before GDP/ R-GDP treatment | Stage 1 (n: 4); Stage 2 (n: 13); Stage 3(n: 16); Stage 4 (n: 36) |
| Bone marrow involvement | 3/38 (8%); 8/31 (25.8%) |
| GDP/R-GDP number of cycles | 2 (n: 36); 3 (n: 26); 4 (n: 7) |
| GDP/R-GDP treatment response | Chemorefractory disease n: 17; Chemosensitive disease n: 52 |
| Stem cell mobilization with GDP/R-GDP | n: 52 (n: 51, 98% successful; n: 1, 2% unsuccessful) |

HL; Hodgkin’s lymphoma, NHL; Non-Hodgkin’s lymphoma.

Table 2. Clinical characteristics of patients.

| Clinical characteristics         | Number of patients (n) |
|----------------------------------|------------------------|
| Lymphoma type                    | 69                     |
| Hodgkin’s lymphoma               | 38                     |
| Non-Hodgkin’s lymphoma           | 31                     |
| Diffuse large B-cell lymphoma    | 24                     |
| T-cell lymphoma                  | 4                      |
| Mantle cell lymphoma             | 1                      |
| Follicular lymphoma              | 1                      |
| Marginal zone lymphoma           | 1                      |
| Previous chemo-therapies         |                        |
| Hodgkin’s lymphoma               |                        |
| ABVD                             | 27                     |
| ABVD + radiotherapy              | 11                     |
| Non-Hodgkin’s lymphoma           |                        |
| R-CHOP                           | 21                     |
| R-CHOP + radiotherapy            | 3                      |
| CHOP                             | 4                      |
| R-EPOCH                          | 2                      |
| CHOEIP                           | 1                      |

ABVD; adriamycin, bleomycin, vinblastine, dacarbazine, R-CHOP; rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOP; cyclophosphamide, doxorubicin, vincristine, and prednisone, R-EPOCH; rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin. CHOEIP, cyclophosphamide, daunorubicin, vincristine, etoposide, prednisone.

Table 3. Results of peripheral blood stem cells collection.

| Variable                                                             | All patients, n: 52 |
|---------------------------------------------------------------------|---------------------|
| Median CD34* cell count in peripheral blood (/μL) (range)           | 55.04 (11.07–467.18) |
| Median apheresis days (range)                                       | 15 (11–20)          |
| Leukapheresis procedure count (n)                                   | 1 (n: 34); 2 (n: 15); 3 (n: 2) |
| Median total CD34* cells collected (10^6/kg) (range)                | 8.68 (4.06–41.50)   |
| Out of target (< 2 × 10^6 CD34 + cells/kg) (%)                      | 1 (2)               |
| Above minimum target (> 2×10^6 CD34 + cells/kg) (%)                 | 51 (98)             |
| Above optimal target (> 5×10^6 CD34 + cells/kg) (%)                | 48 (92)             |

Data are presented as number (n or %) or median (minimum-maximum), where appropriate.

Table 4. Demographic and clinical characteristics of successfully mobilized patients.

| Variable                               | All patients, n: 51 |
|----------------------------------------|---------------------|
| Median age (range)                     | 44 (18–77)          |
| Sex                                    | Male (n: 29); Female (n: 22) |
| Diagnosis                              | HL (n: 24); NHL (n: 27) |
| Disease status                         | Relapse (n: 22); Refractory (n: 29) |
| Stage 1–2, n                           | 15                  |
| Stage 3–4, n                           | 36                  |
| Patients undergoing radiotherapy, n    | 11                  |
| Median CD34 cell count in peripheral blood (cells?/μL) (range)      | 55.04 (11.07–467.18) |
| Previous line of chemotherapy          | 1 line (n: 45); 2 line (n: 4); 3 line (n: 1); 4 line (n: 1) |

Data are presented as number (n) or median (minimum-maximum), where appropriate.
had NHL. Of these, 22 were relapsed, 29 were refractory, and 15 had early stage and 36 had an advanced stage disease. The patient with unsuccessful mobilization was a 25-year-old female relapse Stage 3BX HL who had received one-line chemotherapy before and had a history of RT. Her response to GDP was a complete response. After nearly 3 weeks, CD34+ stem cells were collected with a G-CSF plus plerixafor.

Blood parameters at the collection date are shown in Table 5. The PLT count was below 150 × 10⁹/L in 42 (82%) of 51 patients and below 100 × 10⁹/L in 34 (67%) of 51 patients. 2 patients (4%) had neutropenia (< 1.500 × 10⁹/L).

Grade 1–2 toxicity was approximately 5.9% (n: 3), which was ototoxicity, mucositis, and/or nephrotoxicity. Grade 3–4 toxicity was approximately 7.8% (n: 4), which was neutropenia (n: 2), febrile neutropenia (n: 1), infections requiring hospital admission (n: 2) and/or nephrotoxicity (n: 1).

Patients under 60 years of age had a higher number of CD34+ stem cells collected on day 1 than those over 60 years of age (P: 0.03). However, there was no difference in total CD34+ collected. The amount of premobilization PLT, apheresis day PB CD34 in total CD34, CD34+ total in HL patients were higher than in the NHL patients (P: 0.02, P: 0.002, P: 0.006, P: 0.03, respectively). In the early-stage patients, total CD34+ amount, and apheresis day PB CD34+ was found higher than in the late-stage patients (P: 0.02 and P: 0.04, respectively). As shown in Tables 6 and 7, when patients who received RT were compared with those who did not receive RT, no statistically significant difference was found in terms of WBC, PLT, and premobilization PB CD34+ stem cell counts, total number of collected CD34+ stem cells, number of CD34+ stem cells collected on the 1st day, and apheresis procedures.

### 4. Discussion

Currently, the number of 2 × 10⁶ CD34+ cells/kg is generally considered to be the minimum stem cell count needed for a successful ASCT. Ideally, the optimum value is generally considered to be > 5 × 10⁹ CD34+ cells/kg, and the sum of collected stem cells below < 2 × 10⁹ CD34+ cells/kg is regarded as mobilization failure [6, 7, 8, 15].

Various chemotherapeutic agents are used in conjunction with G-CSF for stem cell mobilization in ASCT. Chemotherapeutic agents should be both effective against the underlying disease and should also facilitate stem cell mobilization; thus, both cytoreduction and mobilization should be provided together. This is the reason why single agents such as cyclophosphamide, etoposide, cytarabine, etc. are used along with G-CSF for both pretransplant cytoreduction and stem cell mobilization; therefore, combined regimens such as GDP, cisplatin, cytosine arabinoside and dexamethasone (DHAP), doxorubicin, methylprednisolone, high-dose cytarabine and cisplatin

| Variable                      | Median (range) |
|-------------------------------|----------------|
| Leukocyte count (×10⁹/L)       | 14 (2.44–53.6) |
| Hemoglobin level (g/dL)       | 11.2 (7.57–13.4) |
| Platelet count (×10⁹/L)       | 62 (20–181)    |
| Neutrophil count (×10⁹/L)     | 8.7 (1.05–42.74) |

### Table 5. Blood parameters at harvest.

### Table 6. Relationship of mobilization and laboratory parameters with clinical variables.

| Variable                      | Median (min-max) | Age | Diagnosis |
|-------------------------------|------------------|-----|-----------|
|                               |                  | Aged < 60 (n: 39) | Aged ≥ 60 (n: 12) | P value | HL (n: 24) | NHL (n: 27) | P value |
| WBC                           |                  | 13.7 (2.4–53.6)   | 14 (6.6–34.1)     | 0.85    | 15.7 (3.2–53.6) | 10.1 (2.4–46.2) | 0.12 |
| PLT                           |                  | 65.5 (20–181)     | 52 (20–107)       | 0.51    | 73 (30–134)    | 46 (20–181)    | 0.02*|
| PB CD34                       |                  | 73.6 (11.1–467.2) | 35.2 (19.5–213)   | 0.12    | 119.3 (19.5–467.2) | 35.2 (11.1–173.8) | 0.002*|
| CD34 (1st)                    |                  | 6.5 (2.3–41.5)    | 3.6 (1.7–20)      | 0.03*   | 11.5 (2.2–34.3) | 4.3 (1.7–41.5) | 0.006*|
| CD34 (T)                      |                  | 9.5 (4.1–41.5)    | 8.2 (5.5–20)      | 0.31    | 12.4 (4.7–34.3) | 8.3 (4.1–41.5) | 0.03*|
| Apheresis count               |                  | 1 (1–3)           | 2 (1–3)           | 0.12    | 1 (1–2)       | 2 (1–3)       | 0.11 |

WBC: white blood cells, PLT: platelet, PB: peripheral blood, CD34 (1st): first day collected stem cell amount, CD34 (T): total collected stem cell amount.
Table 7. Relationship of mobilization and laboratory parameters with clinical variables.

| Stage        | Early (n: 15) | Late (n: 36) | P value | RT (n:11) | Non-RT (n:40) | P value |
|--------------|---------------|--------------|---------|-----------|---------------|---------|
| WBC          | 17.6 (3.2–53.6) | 12.5 (2.4–46.2) | 0.19    | 14.7 (6.6–34.9) | 12.5 (2.4–53.6) | 0.33    |
| PLT          | 74 (24–134)   | 52 (20–181)  | 0.10    | 97 (36–123)  | 55 (20–181)   | 0.15    |
| PB CD34      | 106.7 (33.1–337.6) | 36.8 (11.1–467.2) | 0.02*   | 132.5 (29.3–399.1) | 50.68 (11.1–467.2) | 0.90    |
| CD34 (1st)   | 10.6 (3.3–20) | 4.9 (1.7–41.5) | 0.09    | 6.5 (2.0–13.3) | 5.95 (1.7–41.5) | 0.98    |
| CD34 (T)     | 12.5 (4.1–20) | 8.3 (4.7–41.5) | 0.04*   | 9.5 (4.7–17.1) | 9.14 (4.1–41.5) | 0.92    |
| Apheresis count | 1 (1–2)     | 1 (1–3)     | 0.33    | 1 (1–2)    | 1 (1–3)      | 0.71    |

WBC; white blood cells, PLT; platelet, PB; peripheral blood, CD34 (1st); first day collected stem cell amount, CD34 (T); total collected stem cell amount.

(ASHAP), Vinorelbine, gemcitabine, procarbazine and prednisone (ViGePP) and ifosfamide, carboplatin, and etoposide phosphate (ICE) have been used as stem cell mobilizing regimens in hematology units [16–18]. By using salvage chemotherapy in patients with relapsed or refractory HL, failure of 3%, 18%, and 14% mobilization rates were reported for GDP, carmustine cytarabine etoposide melphalan (Mini-BEAM), and ICE, respectively [16,17].

Bozdağ et al. investigated the effect of chemotherapy regimens on mobilization in lymphoma patients [18]. Patients were given chemotherapy protocols such as cyclophosphamide (n: 15), ASHAP (n: 11), and ViGePP (n: 12) [18]. Although no difference was reported between the groups concerning the number of stem cells collected (P: 0.58), mobilization failure was 33% in the cyclophosphamide group (n: 5/15), 9% in the ASHAP group (n: 1/11) and 8% in the ViGePP group (n: 1/12) [18].

Berber et al. evaluated the effectiveness of the DHAP regimen plus filgrastim for mobilization of stem cells in relapsed and/or refractory lymphoma patients [19]. Stem cells from 32 patients (94%) were collected on the 11th day (1.7–41.5) [19]. Mobilization failure in salvage treatments was reported as 10% in diffuse large B-cell lymphoma (DLBCL) (n: 197) patients given R-ICE, and it was 8% in DLBCL (n: 191) patients given R-DHAP [20]. Moccia et al. provided GDP salvage treatment to 235 relapsed and refractory HL and NHL patients in their study [21]. Autologous stem cell transplantation was applied to 126 patients (69 HL and 57 DLBCL) in total [21]. In addition, Moccia AA et al. also reported GDP as an effective out-patient salvage regimen for relapsed and refractory DLBCL and HL. However, in the study, the effectiveness of GDP on PBSC mobilization has not been adequately evaluated [21].

In the current study, we evaluated the efficacy of the GDP/R-GDP regimen plus G-CSF to mobilize PBSCs in relapsed and refractory lymphoma patients. Successful mobilization was achieved in 51 of chemosensitive patients and approximately 98% of patients had stem cells collected over 2 × 10^6 cells/kg. Our mobilization failure was nearly 2%, and our mobilization failure seemed to be lower when compared to the reports of Mini-BEAM, ICE, cyclophosphamide, ASHAP, ViGePP, R-ICE, and R-DHAP regimens usage reported previously [15–18]. Besides, our study suggests that GDP mobilization regimen may be more effective in HL patients in comparison to NHL patients in terms of premobilization PLT levels, PB CD34 stem cell counts, first-day collected stem cell amount of the mobilization, and the total number of CD34+ stem cells collected as shown in Tables 6 and 7.

Plerixafor could be added to G-CSF at a dose of 24 µg/kg when there is a possibility of inadequate mobilization (defined as PB CD34+ stem cell number < 10 cells/L on the first apheresis day planned or target CD34+ stem cell yield on the first day of apheresis < 50%) [23,24]. Tang C et al. used 4% and 18% plerixafor in regimens (CE (cyclophosphamide/etoposide) + G-CSF and GDP + G-CSF), respectively [24]. Besides, they reported the mobilization failure as 1.2% [24]. In our study, mobilization failure was 2% and only 1 patient used G-CSF plus plerixafor. Eventually, GDP regimen seemed not to need very high rates of plerixafor usage.

Patient and disease-related factors predicting mobilization failure are being over 60 years of age, having...
an underlying advanced disease, having previously received more than one-line chemotherapy, and having low CD34+ cells in peripheral blood before apheresis. However, the low PLT count before mobilization and previous treatments, including fludarabine, melphalan, or lenalidomide are controversial factors in terms of mobilization failure. It is generally accepted that the most influential predictive factor for mobilization failure is the number of CD34+ cells in preapheresis PB [6].

From a total of 145 patients, 52% of whom were diagnosed with lymphoma, participated in a study conducted by Demiriz et al. [25]. The patients were divided into two groups according to successful and unsuccessful mobilization and the groups were compared in terms of the parameters affecting the mobilization success [25]. Among the factors of age, platelet count, LDH, ferritin, CRP, LDL, and triglyceride levels, it was only high platelet count that was shown to be effective in mobilization success in their study (P < 0.05) [25]. On the other hand, due to the high platelet count before mobilization, the number of stem cells collected in HL patients was found to be higher than in NHL patients in this study and it would be an indicator of bone marrow reserve.

Dogu MH et al. showed that age, the number of chemotherapy cycles taken before mobilization, and radiation therapy had no significant effect on the number of final CD34+ stem cell yield (P: 0.492, 0.746, and 0.078, respectively) [26]. On the contrary, in our study, the amounts of CD34+ stem cells collected on the 1st day in patients under 60 years of age and older than that were different; however, total amounts of collected CD34+ stem cells were similar. However, there was no difference in terms of the amount of collected total CD34+ between the patients who received RT and those who did not. In addition, when early stage patients were compared with late stage patients, the total number of collected CD34+ stem cells was found to be significantly higher in the early stage patients.

Tang C et al. examined the efficacy and safety of PBSC mobilization following CE + G-CSF versus GDP + G-CSF [24]. Patients mobilized with CE + G-CSF required fewer days of leukapheresis (median 1 vs. 2 days; P: 0.001) and achieved a higher total CD34+ stem cell yield than patients mobilized with GDP + G-CSF (8.5 × 10⁶ vs. 7.1 × 10⁶ CD34+ cells/kg; P: 0.001) [24]. Frequencies of febrile neutropenia and rates of CD34+ stem cell collection ≥ 5 × 10⁶ CD34+ cells/kg were similar [24]. Furthermore, in our study, GDP/R-GDP regimens provided a median number of 8.68 × 10⁶ cells?/kg of CD34+ stem cells (range 4.06–41.50) PBSCs. Total CD34+ stem cell yield was collected by one leukapheresis procedure in 34 (= 66.7%) patients, 2 leukapheresis procedures in 15 patients (= 29.4%), and 3 leukapheresis procedures in 2 (= 3.9%) patients.

In conclusion, we observed acceptable hematological and nonhematological toxicities with R-GDP/GDP salvage chemotherapies used in relapsed and refractory lymphoma patients. We also showed high rates of successful stem cell mobilization in relapsed and refractory lymphoma patients receiving GDP/R-GDP salvage chemotherapies. Therefore, GDP/R-GDP chemotherapy regimens should also be kept in mind as an alternative for salvage chemotherapy followed by peripheral stem cell mobilization in patients with relapsed and refractory lymphoma. It can also be assumed that a GDP mobilization regimen may be more effective, especially in patients with early-stage disease and also HL patients.

Conflicts of interest
The authors declared that there is no conflict of interest in this study.

Ethical approval
Local ethics committee approval was obtained.

References
1. Schmitz N, Pfistner B, Sextro M, Sieber M, Carella AM et al. Aggressive conventional chemotherapy compared with high-dose chemotherapy with autologous haemopoietic stem-cell transplantation for relapsed chemosensitive Hodgkin's disease: a randomised trial. The Lancet 2002; 359 (9323): 2065-2071. doi: 10.1016/S0140-6736(02)08938-9

2. Ozkan HA, Bal C, Gulbas Z. Chemomobilization with high-dose etoposide and G-CSF results in effective and safe stem cell collection in heavily pretreated lymphoma patients: report from a single institution study and review. European Journal of Haematology 2014; 92 (5): 390-397.

3. Beyer J, Schwella N, Zingsem J, Strohscheer I, Schwaner I et al. Hematopoietic rescue after high-dose chemotherapy using autologous peripheral-blood progenitor cells or bone marrow: a randomized comparison. Journal of Clinical Oncology 1995; 13 (6): 1328-1335. doi: 10.1200/JCO.1995.13.6.1328

4. Richman CM, Weiner RS, Yankee RA. Increase in circulating stem cells following chemotherapy in man. Blood 1976; 47: 1031-1039.

5. Weaver CH, Schwartzberg LS, Birch R, Greco FA, Rhinehart S et al. Collection of peripheral blood progenitor cells after the administration of cyclophosphamide, etoposide, and granulocyte-colony-stimulating factor: an analysis of 497 patients. Transfusion 1997;37 (9):896-903. doi: 10.1046/j.1537-2995.1997.37997454014.x
6. Mohty M, Hübel K, Kröger N, Aljurf M, Apperley J et al. Autologous haematopoietic stem cell mobilisation in multiple myeloma and lymphoma patients: a position statement from the European Group for Blood and Marrow Transplantation. Bone Marrow Transplantation 2014; 49 (7): 865-872. doi: 10.1038/bmt.2014.39

7. Stiff PJ, Micallef I, Nademanee AP, Stadmayer EA, Mazzarz R et al. Transplanted CD34(+) cell dose is associated with long-term platelet count recovery following autologous peripheral blood stem cell transplant in patients with non-Hodgkin lymphoma or multiple myeloma. Biology of Blood and Marrow Transplantation 2011; 17 (8): 1146-1153. doi: 10.1016/j.bbmt.2010.11.021

8. Giralt S, Costa L, Schriber J, Dipersio J, Maziarz R et al. Optimizing autologous stem cell mobilization strategies to improve patient outcomes: consensus guidelines and recommendations. Biology of Blood and Marrow Transplantation 2014; 20 (3): 295-308. doi: 10.1016/j.bbmt.2013.10.013

9. Nakasone H, Kanda Y, Ueda T, Matsumoto K, Shimizu N et al. Retrospective comparison of mobilization methods for autologous stem cell transplantation in multiple myeloma. American Journal of Hematology 2009; 84 (12): 809-814. doi: 10.1002/ajh.21552

10. Pusic I, Jiang SY, Landua S, Uy GL, Rettig MP et al. A risk-based approach to optimize autologous hematopoietic stem cell (HSC) collection with the use of plerixafor. Bone Marrow Transplantation 2012; 47 (4): 483-487. doi: 10.1038/bmt.2011.133

11. Hübel K. Mobilization and collection of HSC. In: Carreras E, Dufour C, Mohty M et al., editors. The EBMT handbook. Hematopoietic stem cell transplantation and cellular therapies. Cham, Switzerland: Springer Nature Switzerland AG; 2019. pp. 117-122.

12. To LB, Levesque JP, Herbert KE. How I treat patients who mobilize hematopoietic stem cells poorly. Blood 2011; 118 (17): 4530-4540.

13. Ford CD, Green W, Wareski S, Petersen FB. Effect of prior chemotherapy on hematopoietic stem cell mobilization. Bone Marrow Transplantation 2004; 33 (9): 901-905.

14. Van Heertum RL, Scarambolo R, Wołodzko JG, Klencke B, Messmann R et al. Lugano 2014 criteria for assessing FDG-PET/CT in lymphoma: an operational approach for clinical trials. Drug Design, Development and Therapy 2017; 13 (11): 1719-1728. doi: 10.2147/DDDT.S136988

15. Olivieri A, Marchetti M, Lemoli R, Tarella C, Iacone A et al. Proposed definition of ‘poor mobilizer’ in lymphoma and multiple myeloma: an analytic hierarchy process by ad hoc working group Gruppo Italiano Trapianto di Midollo Osseo. Bone Marrow Transplantation 2012; 47 (3): 342-351. doi: 10.1038/bmt.2011.82

16. Kuruvilla J, Nagy T, Pintilie M, Tsang R, Keating A et al. Similar response rates and superior early progression-free survival with gemcitabine, dexamethasone, and cisplatin salvage therapy compared with carmustine, etoposide, cytarabine, and melphalan salvage therapy prior to autologous stem cell transplantation for recurrent or refractory Hodgkin lymphoma. Cancer 2006; 106 (2): 353-360.

17. Moskowitz CH, Nimer SD, Zelenetz AD, Trippett T, Hedrick EE et al. A 2-step comprehensive high-dose chemoradiotherapy second-line program for relapsed and refractory Hodgkin disease: analysis by intent to treat and development of a prognostic model. Blood 2001; 1; 97 (3): 616-623. doi: 10.1182/blood.v97.3.616

18. Bozdag SC, Tekgunduz E, Durgun G, Sarica A, Demiriz IS et al. Which regimen is better for stem cell mobilization of lymphoma patients? Transfusion and Apheresis Science 2013; 48 (3): 407-410. doi: 10.1016/j.transci.2013.04.027.

19. Berber I, Erkurt MA, Kuku I, Kaya E, Bag HG et al. DHAP plus florigastim as an effective peripheral stem cell mobilization regimen for autologous stem-cell transplantation in patients with relapsed/refractory lymphoma: a single center experience. Transfusion and Apheresis Science 2016; 54 (1): 48-52. doi: 10.1016/j.transci.2016.01.012

20. Gisselbrecht C, Glass B, Mounier N, Singh Gill D, Linch DC et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. Journal of Clinical Oncology 2010; 20; 28 (27): 4184-4190. doi: 10.1200/JCO.2010.28.1618

21. Moccia AA, Hitz F, Hoskins P, Krasa R, Power MM et al. Gemcitabine, dexamethasone, and cisplatin (GDP) is an effective and well-tolerated salvage therapy for relapsed/refractory diffuse large B-cell lymphoma and Hodgkin lymphoma. Leukemia & Lymphoma 2017; 58 (2): 324-332. doi: 10.1080/10428194.2016.1193852

22. Abhyankar S, DeJarnette S, Aljitawi O, Ganguly S, Merkel D et al. A risk-based approach to optimize autologous hematopoietic stem cell (HSC) collection with the use of plerixafor. Bone Marrow Transplantation 2012; 47 (4): 483-487. doi: 10.1038/bmt.2011.133

23. Kouroukis CT, Varela NP, Bredeson C, Kuruvilla J, Xenocostas A. Plerixafor for autologous stem-cell mobilization and transplantation for patients in Ontario. Current Oncology 2016; 23 (4): e409-e430. doi: 10.3747/co.23.3137

24. Tang C, Espin-Garcia O, Prca A, Kurkreti V, Kriden R et al. Efficacy and safety of stem cell mobilization following gemcitabine, dexamethasone, cisplatin (GDP) salvage chemotherapy in patients with relapsed or refractory lymphoma. Leukemia & Lymphoma 2020; 1: 1-8. doi: 10.1080/10428194.2020.1762882
25. Demiriz İŞ, Bozdağ SC, Tekgündüz E, Uğur B, Durgun G et al. Predicting the successful peripheral blood stem cell harvesting. Transfusion and Apheresis Science 2013; 48 (3): 411-414. doi: 10.1016/j.transci.2013.04.028

26. Doğu MH, Çağırgan S, Ocakci S, Kaya AH, Ilkkilic K et al. Autologous stem cell transplantation and stem cell mobilization kinetics in elderly patients with B cell non-Hodgkin lymphoma. Transfusion and Apheresis Science 2017; 56 (6): 814-818. doi: 10.1016/j.transci.2017.11.012