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ORIGINAL RESEARCH

Salvage Therapy for Relapsed/Refractory Testicular Germ Cell Tumors: King Faisal Hospital and Research Center, Riyadh Experience

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Purpose: Optimal salvage treatment for relapsed/refractory germ cell tumors in men remains controversial. The options include conventional-dose chemotherapy (CDCT) and high-dose chemotherapy with autologous stem cell transplantation (HDCT–ASCT). There is currently a lack of data from the Middle East on this topic. This study presents the largest single-institution experience in the region.

Methods: We retrospectively examined patients aged 14 years or older, treated at King Faisal Hospital and Research Center, Riyadh, between 2010 and 2022. Patients previously received first-line, cisplatin-based chemotherapy. The treatment consisted of either CDCT or HDCT–ASCT. The primary endpoints were event-free survival (EFS) and overall survival (OS).

Results: Study included 46 patients, of whom 24 and 22 received CDCT and HDCT–ASCT, respectively. Using the IPFSG prognostic model as per local institutional practice, patients in the very low, low, and intermediate risk groups received CDCT. In the 24-patient CDCT group, 16 (66%) were high/very high risk, and only 2 (8%) demonstrated primary refractoriness. Contrarily, of the 22 patients who received HDCT–ASCT, 20 (91%) were classified as high/very high risk, and 17 (77%) were primary refractory to first-line treatment. The HDCT-ASCT cohort was heavily weighted toward high/very high risk. HDCT-ASCT group (59%) had a higher complete remission rate than the CDCT group (59% vs 41%). With a median follow-up of 35 months, the 3-year OS was 60% in the CDCT group and 53% in the HDCT-ASCT group, whereas the 3-year EFS rates were 54% and 43%, respectively.

Discussion: Results indicated that HDCT–ASCT achieved a superior response rate compared with CDCT, despite an adverse prognostic profile and numerically comparable survival outcomes with the lower-risk cohort treated with CDCT. These findings suggest that the selection of higher-risk patients for a more intensive therapy is an effective strategy. However, direct comparison is limited by the retrospective nature.

Keywords: testicular germ cell tumor, salvage therapy, autologous stem cell transplant, conventional-dose chemotherapy

Introduction

Testicular cancer is a common and curable type of cancer in men aged 15–35 years. The International Germ Cell Cancer Collaborative Group (IGCCCG) score classifies patients into three risk groups at diagnosis: good, intermediate, and poor.[1] Cisplatin-based chemotherapy cures 60–80% of patients, including those with advanced disease, depending on their clinical stage and IGCCCG risk group. In cases of relapse, the International Prognostic Factors Study Group (IPFSG) proposed outcome prediction using a prognostic model, which is calculated based on the primary site and histology, response to previous treatment, progression-free interval, tumor markers in salvage situations, and the presence of liver, bone, or brain metastases. There are five prognostic groups very low, low, intermediate, high, and very high risk.[2] Relapse that occurs 4 weeks following platinum-based treatment is considered indicative of platinum-refractory

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disease.[3] Treatment of relapses following cisplatin-based chemotherapy and potential residual mass resection is more complex. Patients receive either cisplatin-based conventional dose chemotherapy (CDCT) or high-dose chemotherapy followed by autologous stem cell transplantation (HDCT-ASCT). Various studies have described single and sequential HDCT–ASCT methods.[4] Most centers use high-dose carboplatin and etoposide sequentially, as this is associated with a more favorable toxicity profile based on a prospective Phase 3 trial.[5] To date, it remains unclear whether HDCT–ASCT is the preferred salvage treatment approach in the first relapse. This study reports the largest single-center Middle East experience of managing patients with testicular cancer who have received salvage second-line CDCT or HDC-ASCT. It also presents the clinical manifestation, diagnosis, treatment, event-free survival (EFS), and overall survival (OS).

Materials and Methods

Selection of Patients

We retrospectively identified all male patients with relapsed and/or refractory germ cell tumors (GCTs) who presented between 2010 and 2022 to the center of Adult Medical Oncology and met the eligibility criteria for this analysis from the hospital-wide tumor registry at the King Faisal Specialist Hospital & Research Centre (KFSH&RC) in Riyadh, Saudi Arabia. It is a tertiary healthcare referral center and research institution in Saudi Arabia, with a dedicated Oncology Centre that is considered the largest in the Middle East region. The inclusion criteria were (i) a minimum age of 14 years, with metastatic seminoma or non-seminoma GCT, as defined by pathology or tumor markers; (ii) receiving cisplatin-based first-line chemotherapy; (iii) disease progression or relapse following the initial treatment, confirmed by histology or radiology and rising tumor markers; (iv) receiving cisplatin-based salvage chemotherapy (CDCT); and (v) receiving high-dose chemotherapy and autologous stem cell transplantation (HDCT-ASCT).

This proposal was conducted in accordance with the ethical principles of the Declaration of Helsinki. The Institutional Research Advisory Council of King Faisal Specialist Hospital and Research Centre granted formal approval. The study is registered under RAC approval number #2231-070, and informed consent was obtained from patients and their guardians before the administration of any treatments. Electronic medical records were reviewed. The team used the IPFSG criteria to stratify salvage treatment. Alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (HCG), and lactate dehydrogenase (LDH) were the collected tumor markers. As per local institutional practice, patients in the very low, low, and intermediate risk groups received CDCT, and only HDC–ASCT was offered to intermediate, high-risk, or very high-risk patients.

The internal electronic medical records yielded all variables, including patient demographics, diagnosis details, treatment regimens, and key laboratory measurements. Throughout the entire 12-year study period (2010–2022), the central, standardized laboratory of KFSH&RC performed all routine clinical laboratory measurements, including serum tumor marker levels (AFP, beta-HCG, and LDH). This centralized testing uses standardized institutional protocols to ensure comparability and validation of measurements over the study period.

Salvage Chemotherapy, HDC, and Stem Cell Mobilization

According to local institutional guidelines, salvage treatment involved either CDCT or HDCT–ASCT, followed by residual tumor resection as clinically indicated. The standard CDCT salvage regimen included four cycles of TIP (Paclitaxel, Ifosfamide, Cisplatin): a conventional-dose regimen administered in 21-day cycles. A typical schedule is Paclitaxel (eg, 175 mg/m^2) on Day 1, followed by Ifosfamide (eg, 1.0 g/m^2/day) and Cisplatin (eg, 20 mg/m^2/day) for five consecutive days. Mesna 500 mg/m^2 was given before the ifosfamide and at 4 and 8 hours afterward daily.[6] For HDCT–ASCT, the Memorial Sloan Kettering Cancer Center protocol was used, which is the TI-CE protocol. This multi-stage regimen begins with two cycles of TI (Paclitaxel 200 mg/m^2 on Day 1 and Ifosfamide 2000 mg/m^2/day from Days 1–3) to mobilize stem cells, which are then collected. This is followed by three cycles of high-dose CE (Carboplatin AUC = 8 and Etoposide 400 mg/m^2/day from Days 1–3) every 21 to 28 days, with the previously collected stem cells re-infused after each high-dose cycle.[7] Standard antiemetic and hydration protocols were followed. All patients in each respective group received the same treatment.

Statistical Analysis

The primary endpoints were EFS, calculated from the start of salvage treatment until relapse, progression, or all-cause mortality, and OS, defined as the interval between the initiation of second-line chemotherapy and either the last follow-up or death. Both were estimated using the Kaplan–Meier method. Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 25 (IBM SPSS Statistics, Armonk, NY: IBM Corp). The Log rank test was used to compare survival curves between the two treatment groups. Univariate correlation between prognostic factors and survival was investigated using Cox Proportional-Hazards regression. Given the retrospective nature of the study, any missing data for specific variables were addressed by listwise deletion (excluding the patient from that specific analysis).

Results

The entire cohort of 46 patients was included in the survival analysis from the start of salvage treatment. A total of 24 (52%) patients received CDCT as the first salvage treatment, and 22 received HDCT and ASCT; the details are presented in Table 1. Since it's a retrospective study, direct comparison between the two cohorts was not performed.

Table 1 Baseline Characteristics

Age (median, range)	30 (15–48 years)
Seminoma	6 (13%)
Nonseminoma	40 (86%)
IGCCC risk (at the time of diagnosis)	
Good	9 (19.5%)
Intermediate	11 (24%)
Poor	26 (56.5%)
Metastasis at diagnosis	
Lung	23 (50%)
Brain	1 (2%)
Liver	10 (22%)
No Metastases	5 (11%)
Nodal metastasis	23 (50%)
Tumor markers at the end of the first-line chemotherapy	
Beta HCG > 1000	20 (43.4%)
LDH > 2ULN	17 (37%)
AFP > 100	15 (32%)
Risk category per IPFSG criteria (N = 46)	
Very low/low	5 (11%)
Intermediate	5 (11%)
High/very high	36 (78%)

(*Continued*)

Table 1 (Continued).

Survival/disease status after salvage therapy	
Alive with no disease	21 (45%)
Alive with residual mass	3 (7%)
Alive with disease	4 (9%)
Died of disease	17 (37%)
Died of other causes	1 (2%)
Survival/disease status after CDCT therapy (24 pts)	
IPFSG score high/very high risk	16 (66%)
Primary refractory to 1st line	2 (8%)
Alive with no disease	9 (38%)
Alive with residual mass	3 (12%)
Alive with disease	2 (8%)
Died of disease	10 (42%)
Died of other causes	0
Survival/disease status after HDC and ASCT therapy (22 pts)	
IPFSG score high/very high risk	20 (91%)
Primary refractory to 1st line	17 (77%)
Alive with no disease	11 (50%)
Alive with residual mass	1 (4%)
Alive with disease	2 (9%)
Died of disease	7 (32%)
Died of other causes	1 (5%)

Demographics

The median age of the patients was 30 years (15 to 48 years). A total of 40 patients (87%) were diagnosed with NSGCT, while 6 patients (13%) had seminomatous GCTs (Table 1). At initial presentation, 26 patients (57%) were classified as poor risk, 11 (24%) as intermediate risk, and 9 (19%) as good risk, according to the International Germ Cell Cancer Collaborative Group classification. The tumor marker distribution at the end of first-line chemotherapy showed that 20 patients (43.4%) had beta-HCG levels greater than 1000, 17 (37%) had LDH levels exceeding 2 times the upper limit of normal (ULN), and 15 (32%) had AFP levels above 100. After first-line platinum-based therapy, 8 patients (17%) achieved a complete response (CR), 8 (17%) had a partial response, and 30 (66%) demonstrated primary refractoriness to the initial cisplatin-based chemotherapy.

Second-Line Chemotherapy Details

Metastasis

Notably, 21 of the patients (45%) presented with lung metastasis, 08 (18%) with liver metastasis, and 39 (84%) with nodal metastasis. Moreover, four patients developed brain metastases before the initiation of the second-line chemotherapy.

Prognostic Categories

Using the IPFSG predictive model, the 46 patients were stratified into five risk categories before second-line treatment, based on a score that considers seven prognostic factors. The categories were very low (n = 1), low (n = 4), intermediate (n = 5), high (n = 10), and very high (n = 26). As per local institutional practice, patients in the very low, low, and intermediate risk groups received CDCT. In the 24-patient CDCT group, 16 (66%) were high/very high risk (they received CDCT because the patient refused HDCT-ASCT or based on clinical judgement), and only 2 (8%) demonstrated primary refractoriness. Contrarily, of the 22 patients who received HDCT–ASCT, 20 (91%) were classified as high/very high risk, and 17 (77%) were primary refractory to first-line platinum-based chemotherapy. The HDCT-ASCT cohort was heavily weighted toward high/very high risk. A direct comparison could not be performed owing to the retrospective nature of the study as well as the variations in patient characteristics, disease, and treatment variables between the CDCT and HDCT groups. In the CDCT group, 22 patients (92%) received the TIP regimen (paclitaxel, ifosfamide, and cisplatin), one received the VIP regimen (etoposide, ifosfamide, and cisplatin), and another one received the vinblastine, ifosfamide, and cisplatin regimen as second-line CDCT. In the HDCT-ASCT group overall, 18 patients (82%) underwent three HDCT cycles and ASCT, whereas four (18%) underwent two HDCT cycles and ASCT.

Toxicities

Second-line chemotherapy was well tolerated. However, various side effects were reported, including grade III and grade IV anemia in 7 (15%) and 2 (4%) patients, respectively, and grade III and grade IV neutropenia in 5 (11%) and 10 (21%) patients, respectively. In addition, grade III and IV thrombocytopenia occurred in 9 (20%) and 3 (7%) patients, respectively. In terms of long-term toxicities, only one patient developed Grade I hearing impairment, and one had Grade I peripheral neuropathy in the HDCT-ASCT group.

Response to Second-Line Chemotherapy

Of the 46 patients, 23 (50%) achieved complete remission, whereas 22 (48%) experienced disease progression immediately after or within 3 months of the second-line salvage treatment. One patient achieved biochemical partial remission and was still alive with disease persistence during the last follow-up. Response to conventional-dose chemotherapy.

In the CDCT group, 10/24 (41%) patients achieved biochemical complete remission. Of them, eight also achieved radiological complete remission (CRm-ve). Furthermore, one patient achieved radiological partial remission, which subsequently progressed to sarcoma. Meanwhile, one patient attained biochemical partial remission and was still alive with disease persistence during the last follow-up. A total of 13 patients demonstrated primary refractoriness to CDCT (PDm+ve).

Response to HDCT and ASCT

In HDCT-ASCT, 13 out of 22 (59%) patients achieved biochemical complete remission. Among them, nine also achieved radiological complete remission (CRm-ve). Moreover, radiological partial remission was attained by four patients (PRm-ve), of whom two underwent RPLND (one had teratoma, and the other had residual disease). Two patients did not receive surgical intervention. Meanwhile, nine patients demonstrated primary refractoriness to HDCT–ASCT (PDm+ve); of them, three were alive (one with disease persistence and two were disease free). The rest succumbed to the disease. Univariate correlation between IPFSG prognostic factors and survival, poor survival (P-value < 0.001) with beta-HCG levels >1000 at the time of relapse was observed. However, this analysis remains exploratory given the limited number of events. In our cohort, the CR rate was 41% in the CDCT group (n = 24) and 59% in the HDCT–ASCT group (n = 22).

Post-Salvage Treatment Failure and Management

Of the 46 patients, 22 experienced an event following their second-line treatment. These patients received gemcitabine-based chemotherapy. At the time of the last follow-up, five patients were still alive, three with disease persistence and actively receiving chemotherapy, and two who had achieved CR and are disease-free. One of these patients underwent

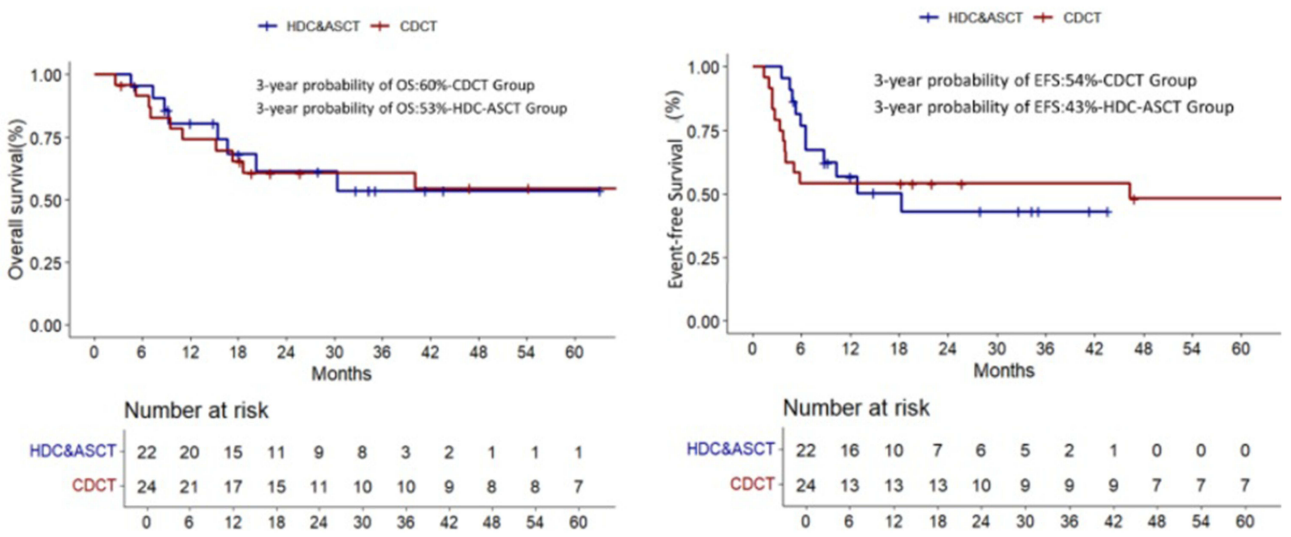

Figure 1 Survival analysis.

chemotherapy followed by salvage surgery and has maintained remission. Unfortunately, 17 of the patients died from the disease, of whom 3 did not receive further treatment, and 14 were treated with chemotherapy.

Survival Analysis

With a median follow-up of 35 months (95% confidence interval [CI], 24–46 months), the entire study cohort demonstrated a 3-year EFS probability of 50.7% (95% CI, 37–68%) and an OS rate of 57% (95% CI, 45–75%). Of the cohort, 28 patients are still alive; 21 are alive without the disease, whereas 17 have died from the disease. The treatment-related mortality was 0%. Further subgroup analysis was not feasible owing to the limited sample size. The HDC–ASCT group had a median EFS of 18.2 months (95% CI, 6.47 months–NA), with a 3-year EFS probability of 43% (95% CI, 25–74%) and an OS rate of 53% (95% CI, 34–85%). The CDCT group had a median EFS of 46 months (95% CI, 4%–NA), with a 3-year EFS probability of 54% (95% CI, 38–78%) and an OS rate of 60% (95% CI, 43–84%). The key finding of our study is that the lower-risk group that received CDCT—of whom only two patients were refractory to first-line platinum-based chemotherapy—showed survival outcomes numerically comparable to those of the HDCT–ASCT group. The higher-risk group who received the more intensive therapy (HDCT–ASCT) also had nearly comparable outcomes (Figure 1).

Discussion

Although cisplatin-based chemotherapy achieves high cure rates in primary testicular cancer, 20–30% of patients relapse,[7] requiring further treatment. For these patients, two main salvage strategies are employed: CDCT and HDC–ASCT. The optimal approach between these two options remains to be determined. Through a large retrospective analysis, the IPFSG established a prognostic risk score that classifies patients into five categories based on seven clinical characteristics. Significant differences were observed in 2-year PFS and 3-year OS rates among the groups. The rates for patients with a very low-risk profile were 75.1% and 77%, and for those with a very high-risk profile were 5.6% and 6.1%, respectively. In addition to the IPFSG score, the rate of decline in serum tumor marker levels within the first 6 weeks of salvage chemotherapy predicts outcomes.[8]

Current use of HDCT-ASCT is based on Phase I and II trials and retrospective studies. The IT94 study[9] is the only published Phase III randomized controlled trial comparing CDCT with HDCT–ASCT, but it failed to demonstrate a significant survival benefit with HDCT–ASCT. Despite several limitations, this study remains the best available evidence on the use of HDCT–ASCT in relapse-refractory GCT. The IT94 study concluded that HDCT–ASCT may enhance EFS in men with relapsed GCTs (hazard ratio, 0.80; 95% CI, 0.59–1.10; P=0.169), with no difference in response rate or OS. However, some limitations remain. For instance, the study excluded patients with refractory disease, so definitive conclusions regarding

resistance to first-line platinum-based chemotherapy could not be drawn. In addition, the study employed only one cycle of HDCT–ASCT, a practice that is now seldom used. Few retrospective studies suggest that HDCT–ASCT is preferable to CDCT. In a retrospective analysis of the IPFSG database, 821 patients who received HDCT–ASCT as first-line salvage treatment were compared with 773 patients who received CDCT. The HDCT–ASCT group had a higher 2-year EFS (55% vs 44.1%, P <0.001) across all five risk groups and a higher OS rate (60.6% vs 46.3%, P <0.001), except for the lowest-risk patients. Beyer et al[10] retrospectively compared HDCT–ASCT with CDCT as first-line salvage treatment in patients with relapsed or refractory nonseminomatous germ cell tumors, indicating a potential benefit of HDCT, with an estimated absolute improvement in EFS of 6–12% and OS of 9–11% at 2 years. Several systematic and literature reviews have been published on this topic and yielded varying results. In Table 2, the findings of HDC–ASCT studies conducted at leading institutions known for treating relapse-refractory testicular cancer patients are briefly summarized. Our study found that 50% of patients achieved complete remission, with 3-year OS rates of 60% and 53% in the CDCT and HDC–ASCT groups, respectively, which align with the results of the majority of the aforementioned retrospective studies. Although the HDCT–ASCT group had more cases refractory to first-line chemotherapy and more adverse prognostic features based on the IPFSG score, it achieved a higher response rate and comparable survival outcomes. This is a key finding of our study, suggesting that a more intensive therapy is

Table 2 HDC–ASCT Studies Conducted at Leading Institutions

Author (Year)	Study Design	N	Notable I/E Criteria	Median f/u (m)	HDCT as Initial Salvage	HDCT Regimen	Cycles	Event Free Survival	OS
Einhorn et al[13]	Retrospective (Indiana Uni)	184	I: None E: PM-NSGCT and late relapse	48	73%	Carboplatin 700 mg/m^2 (d1–3) Etoposide 750 mg/m^2 (d1–3)	2	58% 2-year DFS	65% at 5 years
Feldman et al[7]	Prospective, phase I/II (MSKCC)	107	I: ≥1 Adverse prognostic feature for salvage CDCT E: None	61	76%	Part A (TI): Paclitaxel 200 mg/m^2 (d1) Ifosfamide 2000 mg/m^2 (d1–3)	2	48% 5-year DFS	52% at 5 years
						Part B (CE): Carboplatin AUC 7–8 (d1–3) Etoposide 400 mg/m^2 (d1–3)	3		
Lorch et al[5]	Prospective, randomized phase III (German)	211	I: None E: None	90	86%	Arm A: • VIP • Carboplatin 500 mg/m^2 (d1–3) • Etoposide 500 mg/m^2 d (1–3)	1 3	52% 2-year PFS	50% at 5 years
						Arm B: • VIP • Carboplatin 550 mg/m^2 (d1–4) • Etoposide 600 mg/m^2 (d1–4) • Cyclophosphamide 1600 mg/m^2 (d1–4)	3 1	47% 2-year PFS	40% at 5 years
Adra et al[11]	Retrospective (Indiana Uni)	364	I: None E: Late relapse	40	83%	Carboplatin 700 mg/m^2 (d1–3) Etoposide 750 mg/m^2 (d1–3)	2	60% 2-year PFS	66% at 5 years

(*Continued*)

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Table 2 (Continued).

Author (Year)	Study Design	N	Notable I/E Criteria	Median f/u (m)	HDCT as Initial Salvage	HDCT Regimen	Cycles	Event Free Survival	OS
Keskin et al[12]	Retrospective (Single-Center Experience In Ankara, Turkey)	133	I: Age ≥18 years at the time of HDCT. Patients progress radiologically/ biochemically after first-line standard cisplatin treatment/underwent surgery for residual disease then relapsed. E: Patients with insufficient follow-up time.	31.1	100%	Part 1 (TIP): Paclitaxel 250 mg/m^2/ day d1 Ifosfamide and mesna 1500 mg/m^2/ day d (2–5) Cisplatin 25 mg/m^2/ day d (2–5)	3	50.3% 2-year PFS	60.8% at 2 years
						Part 2: Carboplatin 700 mg/m^2 d (1–3) Etoposide 750 mg/m^2 d (1–3)	1		
Seidel et al[14]	Retrospective (international multicentric analysis)	283	I: Patients relapse/progress after 3–6 cycles of platinum-based therapy. E: None	27.0	56%	HD-CE*	2–3	Unknown	74% at 2 years and 63% at 5 years
						HD-VIP	Unknown		
						HD-CE with cyclophosphamide	Unknown		
						HD-CE with thiotepa	Unknown		
						HD-ICE	Unknown		

a better strategy for patients with poor prognosis. In our cohort, 48% of patients experienced disease progression within 3 months of completing salvage therapy. While most published real-world studies report progression-free survival over longer intervals, the proportion of patients with early progression in our study is broadly consistent with previously reported outcomes. For example, large retrospective analyses by Lorch et al[6] and Adra et al[11] indicate that overall progression or relapse following salvage therapy occurs in a significant proportion of patients in real-world clinical practice, particularly in cohorts enriched for high-risk features. Similarly, Yildiran Keskin et al[12] reported a 2-year PFS of ~50.3% after high-dose chemotherapy and autologous stem cell transplantation in relapsed/refractory germ cell tumors, with a median time to relapse of approximately 4.8 months among those who progressed, suggesting that many events occur early after salvage therapy.

The limitations of this study include its small, retrospective design. Additionally, some data, particularly on long-term toxicity, were not consistently documented over the 12-year retrospective period. This lack of complete data may potentially lead to an underestimation of the true long-term treatment-related morbidity associated with both CDCT and HDCT–ASCT regimen. However, this missing data did not affect survival, as only one patient died without disease in remission secondary to infection. This highlights the need for prospective studies with standardized, long-term toxicity reporting. Another limitation of this study is the inherent selection bias due to its retrospective design; patients were not randomized; rather, as per the local institutional guidelines allocated patients were allocated only with intermediate- to very high-risk disease, as per the IPFSG criteria, to HDCT-ASCT, Consequently, they had a significantly higher burden of poor prognostic factors. Notably, 91% of the HDCT-ASCT group were high/very high risk, and 77% were refractory to first-line platinum-based chemotherapy, compared to 66% and 8%, respectively, in the CDCT group. Since allocation is not randomized, a direct comparison of the two cohorts is not methodologically valid. No advanced statistical methods, such as propensity score matching, were used to correct for this selection bias due to the limited sample size (N=46) and event count. However, the key finding—that the HDCT-ASCT group achieved numerically comparable survival outcomes (3-year OS 53%) to the lower-risk CDCT cohort (3-year OS 60%) despite a substantially more adverse prognostic profile—suggests the effectiveness of selecting higher-risk patients for a more intensive therapy is a rational institutional strategy.

Conclusion

We present the largest single-institution data from the largest center in the Middle East, a region underrepresented in the experience of managing patients with testicular cancer who have received salvage second-line chemotherapy and HDC–ASCT following disease progression. Our findings suggest that second-line chemotherapy for GCTs in men can lead to long-term disease control. Our experience suggests that HDCT–ASCT yields better response than CDCT and that higher-risk patients should be allocated to the more intensive therapy. The two approaches cannot be directly compared owing to the study's retrospective design, clear selection bias, and limited sample size. This controversial issue of whether CDCT or HDCT is superior as initial salvage therapy will remain unanswered, and our findings cannot be validated until we have the results of the phase III TIGER trial (ClinicalTrials.gov identifier: NCT02375204) published. This trial, which compares TIP with high-dose chemotherapy, will determine the optimal second-line treatment approach. It will include patients with relapsed and refractory testicular GCT and assess the effects of commonly used chemotherapy regimens in this setting (ie, TI–CE followed by ASCT vs TIP). In addition, it will identify patients who benefit most from HDCT followed by ASCT, based on the IPFSG risk classification.

Abbreviations

CR, Complete response; CRm+ve, Complete response marker positive; CRm-ve, Complete response marker negative; PRm +ve, Partial response marker positive; PRm−ve, Partial response marker negative; PDm+ve, Progressive disease marker positive; EFS, Event-free survival; GCT, Germ cell tumors; IGCCCG, International Germ Cell Cancer Collaborative Group; IPFSG, International Prognostic Factors Study Group; OS, Overall survival; SPSS, Statistical Package for the Social Sciences.

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Disclosure

The authors report no conflicts of interest in this work.

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