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ORIGINAL ARTICLE

Multidisciplinary clinic approach improves overall survival outcomes of patients with metastatic germ-cell tumors

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Background: To report our experience utilizing a multidisciplinary clinic (MDC) at Indiana University (IU) since the publication of the International Germ Cell Cancer Collaborative Group (IGCCCG), and to compare our overall survival (OS) to that of the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) Program.

Patients and methods: We conducted a retrospective analysis of all patients with metastatic germ-cell tumor (GCT) seen at IU from 1998 to 2014. A total of 1611 consecutive patients were identified, of whom 704 patients received an initial evaluation by our MDC (including medical oncology, pathology, urology and thoracic surgery) and started first-line chemotherapy at IU. These 704 patients were eligible for analysis. All patients in this cohort were treated with cisplatin–etoposide-based combination chemotherapy. We compared the progression-free survival (PFS) and OS of patients treated at IU with that of the published IGCCCG cohort. OS of the IU testis cancer primary cohort ($n = 622$) was further compared with the SEER data of 1283 patients labeled with 'distant' disease. The Kaplan–Meier method was used to estimate PFS and OS.

Results: With a median follow-up of 4.4 years, patients with good, intermediate, and poor risk disease by IGCCCG criteria treated at IU had 5-year PFS of 90%, 84%, and 54% and 5-year OS of 97%, 92%, and 73%, respectively. The 5-year PFS for all patients in the IU cohort was 79% [95% confidence interval (CI) 76% to 82%]. The 5-year OS for the IU cohort was 90% (95% CI 87% to 92%). IU testis cohort had 5-year OS 94% (95% CI 91% to 96%) versus 75% (95% CI 73% to 78%) for the SEER 'distant' cohort between 2000 and 2014, *P*-value <0.0001.

Conclusion: The MDC approach to GCT at high-volume cancer center associated with improved OS outcomes in this contemporary dataset. OS is significantly higher in the IU cohort compared with the IGCCCG and SEER 'distant' cohort.

Key words: testicular cancer, germ-cell tumor, IGCCCG, multidisciplinary, SEER

Introduction

Germ-cell tumors (GCTs) are the most common cancer in men between 15 and 35 years of age, with an estimated 8720 cases diagnosed annually in the United States and 410 deaths [1]. First-line chemotherapy with bleomycin–etoposide–cisplatin (BEP) became the standard of care for patients with advanced GCT [2–5]. The International Germ Cell Cancer Collaborative Group (IGCCCG) in 1997 published a consensus statement classifying patients with metastatic GCT into good, intermediate, and poor risk disease [6]. Good risk GCT had a 5-year progression-free survival (PFS) of 88% and a 5-year overall survival (OS) of 91%. Intermediate risk GCT had a 5-year PFS of 75% and a 5-year OS of 79%. The poor risk category had a 5-year PFS of 41% and a 5-year OS of 48%.

The optimal management of GCTs is complex, with options including chemotherapy and surgery. At Indiana University Cancer Center (IU), we have established a multidisciplinary clinic (MDC) to evaluate newly diagnosed GCT patients and those needing additional consultation. The goals of this MDC are to provide state-of-the-art oncology care and to educate patients, their families, medical students, residents, and fellows in training. Our MDC integrate dedicated team including medical oncologists, pathologists, urologic and thoracic surgical oncologists, full-time coordinator (responsible for data acquisition, scheduling, and following up with patients and referring physicians) and oncology nurses. The team meets on a weekly basis in a multidisciplinary tumor board. Through this clinic, we can establish the accurate pathologic diagnosis, offer combination chemotherapy, surgical resection of residual tumor and enroll patients on clinical trials all in one visit (supplementary Figure S2, available at *Annals of Oncology* online).

Institutional experience, hospital and physician volume have been associated with improved outcomes of testicular cancer [7–10]. Recent outcome data from large datasets are missing, and the difference in results of patients treated in large volume centers and community centers is unknown. We, therefore, report survival outcomes in 704 consecutive patients with metastatic GCT treated at our MDC at IU since the publication of IGCCCG and compare the outcome to those of National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) Program.

Patients and methods

Patients

The IU Cancer Registry database was queried, and a retrospective review was carried out to compare the PFS and OS of patients treated at IU with that of IGCCCG [6]. This study used the secure Web-based, Title 21 Code of Federal Regulations Part 11—compliant Research Electronic Data Capture (REDCap) system for data input. Eligible patients who had metastatic GCT treated at IU after the establishment of IGCCCG between January 1998 and December 2014 were included. All patients were treated with standard cisplatin–etoposide-based combination chemotherapy consisting of at least three to four cycles of cisplatin and etoposide with or without bleomycin or ifosfamide [11, 12]. SEER Research Data (1973–2014) was also obtained to compare OS of the IU cohort the SEER distant cohort. The SEER distant cohort consisted of patients in the SEER database with testis cancer diagnosed between 2000 and 2014, who had an SEER historical stage of distant, and who had available survival data [13].

Statistical analysis

The end points of the study were the PFS and OS probabilities at 5 years. For the IU cohort, PFS started with the initiation of chemotherapy and ended with progression or death, whichever occurred first. OS started with the initiation of chemotherapy and ended with the death of a patient. Survival status was identified from medical charts or death certificates. Patients without an event were censored at the date of last follow-up. For the SEER distant cohort, OS started with the date of diagnosis and ended with the death of a patient. Patients alive at the date of last contact were censored. PFS and OS were calculated according to the Kaplan–Meier method and using the log-rank test. Analyses were completed compared using SAS software, version 9.4 and figures were created in R, version 3.3.2. Five-year PFS and OS were reported along with 95% confidence intervals (CIs) calculated using the log–log method.

Results

Patient and disease characteristics

For the IU cohort, 1611 consecutive patients with metastatic GCT were evaluated in the MDC at IU between 1998 and 2014. Of these, 704 patients started the initial chemotherapy at IU and were included in the primary outcome analysis (supplementary Figure S1, available at *Annals of Oncology* online). Median age at diagnosis was 29 (range 13–62). Median follow-up time was 4.4 years. The primary tumor site was testis in 622 (88.4%), retroperitoneum in 26 (3.7%), and mediastinum in 54 (7.7%). Eighty-five percent of patients had nonseminomatous GCT (NSGCT). Ninety-seven percent of patients were white, 1% were black, and the remaining 2% were a variety of races/ethnicities. Of note, we did not include LDH in our database. Elevations in LDH are highly nonspecific and may be found in a vast number of benign and malignant conditions [14]. Table 1 lists patients and disease characteristics at the time of initiation of first-line chemotherapy. Supplementary Figure S3, available at *Annals of Oncology* online, presents a map of the United States showing the zip codes of patients seen at our center.

For the SEER distant cohort, 1283 patients were identified from the SEER database with testis cancer diagnosed between 2000 and 2014. To be included in the cohort, patients must have had an SEER historical stage of distant and available survival data. Patients with a survival time of 0 (i.e. date of diagnosis and date of last contact are the same) were excluded. Median age at diagnosis was 32 (range 0–87). Eighty-seven percent of patients were white, 5% were black, and the remaining 8% were a variety of races/ethnicities. A 73.5% of patients had NSGCT.

Treatment administration

All 704 assessable patients in the IU cohort were treated with cisplatin–etoposide combination chemotherapy. Details regarding first-line treatment regimen stratified per IGCCCG risk classification are listed in Table 1. Overall, 82% of patients achieved a complete response and remained disease-free after first-line chemotherapy. A total of 250 patients (36%) underwent post-chemotherapy retroperitoneal lymph node dissection (PCRPLND), 129 (18%) thoracic surgery, 21 cervical lymph node dissection and 9 patients had a resection of brain metastasis. One hundred and fifty-three patients failed first-line chemotherapy, 118 received salvage chemotherapy including high-dose chemotherapy (HDCT) ($n = 76$), and 51 had salvage surgery. At last follow-up, 635 patients (90%) had no evidence of disease (NED), 65 patients (9%) had died, and 4 patients (1%) were alive with relapsed disease. Among patients who died, 52 patients were dead of disease progression, and 13 patients died of other causes including treatment-related toxicity, secondary malignancy, or surgical complications.

We also reviewed the GCT patients who came to IU for a second opinion. Nine hundred and seven patients sought a second opinion or were evaluated after receiving first-line therapy at an outside institution and were not included in the primary analysis.

Table 1. Patient's and disease's characteristics at the beginning of first-line chemotherapy

Characteristic	Overall (*N* = 704)	Good[a] (*N* = 449; 63.8%)	Intermediate[a] (*N* = 74; 10.5%)	Poor[a] (*N* = 181; 25.7%)
Median age (range)	29.3 (13.1–61.5)	30.54 (14.9–61.5)	26.8 (16.0–49.6)	26.9 (13.1–55.7)
Location of primary tumor				
Testis	622 (88.4%)	433 (96.4%)	70 (94.6%)	119 (65.8%)
Retroperitoneum	26 (3.7%)	9 (2.0%)	3 (4.0%)	14 (7.7%)
Mediastinum	54 (7.7%)	5 (1.1%)	1 (1.4%)	48 (26.5%)
Unknown	2 (0.2%)	2 (0.5%)	0	0
Tumor histology				
Seminoma	106 (15.1%)	99 (22.1%)	7 (9.5%)	0
NSGCT	598 (84.9%)	350 (77.9%)	67 (90.5%)	181 (100%)
Predominant histology				
Embryonal	257 (36.5%)	205 (45.7%)	22 (29.7%)	30 (16.6%)
Choriocarcinoma	48 (6.8%)	1 (0.2%)	5 (6.8%)	42 (23.2%)
Yolk sac tumor	69 (9.8%)	16 (3.6%)	9 (12.2%)	44 (24.3%)
Teratoma	65 (9.2%)	29 (6.5%)	7 (9.5%)	29 (16.0%)
Mixed	104 (14.8%)	53 (11.8%)	21 (28.4%)	30 (16.6%)
Seminoma	63 (9.0%)	59 (13.1%)	3 (4.0%)	1 (0.6%)
Pure seminoma	79 (11.2%)	74 (16.5%)	5 (6.8%)	0
Necrosis	11 (1.6%)	5 (1.1%)	2 (2.7%)	4 (2.2%)
IGCN (CIS)	8 (1.1%)	7 (1.6%)	0	1 (0.6%)
Median serum AFP (ng/ml) (range)	10.8 (0.2–280 000)	5.9 (0.2–999)	1323.6 (0.6–9653)	270.3 (0.9–280 000)
Serum AFP				
<1000	578 (82.8%)	444 (100%)	29 (39.2%)	105 (58.3%)
1000–10 000	79 (11.3%)	0	45 (60.8%)	34 (18.9%)
≥10 000	41 (5.9%)	0	0	41 (22.8%)
Median serum HCG (mIU/ml) (range)	21.7 (0–1 700 000)	6.2 (0–4981.9)	1334.5 (0–41 000)	10838.0 (0.5–1 700 000)
Serum HCG				
<5000	571 (81.8%)	444 (100%)	44 (59.5%)	83 (46.1%)
5000–50 000	51 (7.3%)	0	30 (40.5%)	21 (11.7%)
≥50 000	76 (10.9%)	0	0	76 (42.2%)
Metastatic site(s)				
Retroperitoneum	555 (78.8%)	362 (80.6%)	68 (91.9%)	125 (69.1%)
Pulmonary	270 (38.4%)	96 (21.4%)	41 (55.4%)	133 (73.5%)
NPVM	93 (13.2%)	0	5 (6.8%)	88 (48.6%)
Liver	60 (8.5%)	0	1 (1.4%)	59 (32.6%)
Brain[b]	34 (4.8%)	0	3 (4.1%)	31 (17.1%)
Bone[b]	16 (2.3%)	0	2 (2.7%)	14 (7.7%)
Other	12 (1.7%)	0	1 (1.4%)	11 (6.1%)
First-line chemotherapy				
BEPX3	384 (54.6%)	371 (82.6%)	7 (9.5%)	6 (3.3%)
BEPX4	123 (17.5%)	6 (1.3%)	26 (35.1%)	91 (50.3%)
BEPX3+EPX1	69 (9.8%)	15 (3.3%)	33 (44.6%)	21 (11.6%)
EPX4	42 (6.0%)	41 (9.1%)	1 (1.3%)	0
VIPX4	50 (7.1%)	0	2 (2.7%)	48 (26.5%)
Other	36 (5.1%)	16 (3.6%)	5 (6.8%)	15 (8.3%)

[a]Risk per IGCCCG classification.

[b]Brain/bone imaging was not mandatory.

NPVM, nonpulmonary visceral metastasis; IGCCCG, International Germ Cell Cancer Collaborative Group; AFP, alpha fetoprotein; HCG, human chorionic gonadotropin; IU, International unit; NSGCT, nonseminomatous germ-cell tumor; IGCN, intratubular GERM cell neoplasia.

Four hundred and ninety-two (56%) underwent PCRPLND, 432 (51%) underwent salvage chemotherapy, and 172 (21%) underwent thoracic surgery as a result of the multidisciplinary evaluation.

Survival outcomes

With a median follow-up of 4.4 years, the estimated 5-year PFS was 79% (95% CI 76% to 82%) and the 5-year OS was 90% (95% CI 87% to 92%) for the IU cohort (Table 2). The 5-year PFS for

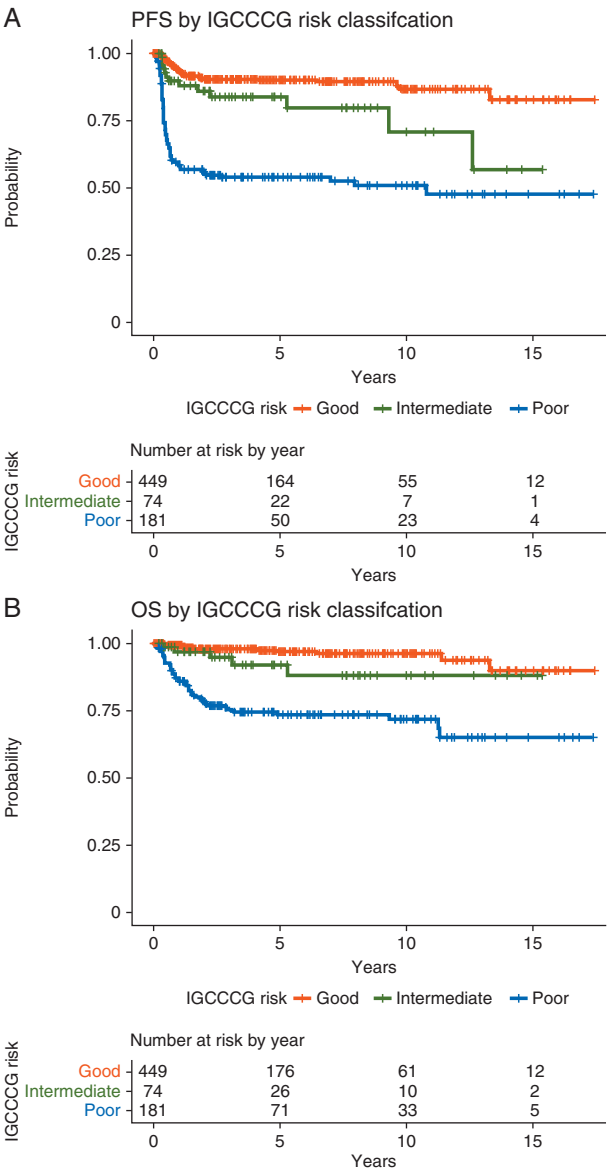

Figure 1. Kaplan–Meier estimates of progression-free survival (A) and overall survival (B) according to IGCCCG risk stratification.

good, Intermediate and poor risk were 90%, 84%, and 54%, respectively (Figure 1A), and the estimated 5-year OS was 97%, 92%, and 73% (Figure 1B), respectively. In sub-segment of patients with testis as the primary site at presentation (IU testis cohort $n = 622$), the 5-year OS was 94% (95% CI 91% to 96%). Patients with primary mediastinal nonseminomatous GCT (PMNSGCT) had an estimated 5-year PFS of 50% (95% CI 35% to 63%) and 5-year OS of 59% (95% CI 43% to 72%). Patients with brain metastasis at diagnosis had an estimated 5-year PFS of 15% (95% CI 5% to 28%) and 5-year OS of 46% (95% CI 28% to 63%).

To demonstrate the impact of our MDC approach, we compared OS of patients in the IU testicular primary cohort with the SEER distant cohort. The 5-year OS for the SEER distant cohort was 75% (95% CI 73% to 78%) compared with 94% (95% CI 91% to 96%) for IU testis cohort (P-value <0.0001; Figure 2). The SEER database does not allow stratification according to the IGCCCG risk category; therefore comparisons of survival between groups are not possible.

Discussion

To our knowledge, this is the largest single-institution study evaluating survival outcomes of patients with metastatic GCT. Survival results of patients treated at IU appear superior to the results of the IGCCCG (Table 2) and the NCI SEER distant cohort (Figure 2). This observation is supported by a large multi-institutional initiative that provided outcome results from high-volume centers that were superior to the original IGCCCG [15]. These data were, however, not directly compared with community outcomes. Several factors may account for excellent survival outcomes seen at our center compared with the IGCCCG and SEER database. This could be attributed to the uniform utilization of cisplatin–etoposide-based combination chemotherapy, improvement in supportive care avoiding delays between cycles, expertise in post-chemotherapy surgical resection of residual disease and the experience resulting from a large volume of patients. Our dedicated multidisciplinary team of medical, urologic and thoracic oncologists, and pathologists have specific academic interest in GCT supported by strong research and clinical trials designed to refine treatment, improve supportive care, and patient education.

Surgical treatment is crucial for the management of metastatic GCT to improve survival and reduce complications [16, 17]. Appropriate patient selection and timing of surgery have lowered morbidity while improving oncologic outcomes at high volume centers [18, 19]. The marked improvement in OS in all-risk categories maybe driven by the development of successful salvage therapy options including salvage surgery, and the long-term experience in HDCT followed by autologous peripheral blood stem-cell transplant [20–25].

This analysis has limitations. This is a retrospective single institution study, and potential bias exists in our patient population. We did not have access to matched patient's characteristics between the contemporary IU cohort and the historical IGCCCG cohort, and the community patients reported in SEER. Referral bias might have affected the results of this study. However, this study has a large sample size of consecutive patients with metastatic GCT treated at a tertiary care center with long follow-up. A large portion of patients enrolled in the study had poor risk disease 25.7% compared with 14% of patients from the IGCCCG [6]; hence survival outcomes for patients treated at other institutions or in the community might vary. Besides, a limitation of this study is that NCI SEER uses a staging system including local, regional, and distant metastases which are not typically used in GCT. The IGCCCG classification of good, intermediate, and poor risk is not included in the SEER database which makes further analysis not possible. That is why we compared all patients with metastatic disease as one group.

Despite substantial improvement in outcomes of patients with metastatic GCT treated in the modern era, many challenges remain. There is a clear disparity in health care outcomes among patients with testis cancer [26–28]. This could be related to patient's factors such as under insurance, poor socioeconomic status, ethnicity, and a language barrier that delays diagnosis.

Table 2. Comparison of survival outcomes between the IGCCCG, IU and NCI SEER dataset

Risk per IGCCCG criteria	5-Year	Indiana University 1998–2014 (%)	IGCCCG 1975–1990 (%)	NCI SEER 2000–2013 (%)
Good risk	PFS	90	88	NA
	OS	97	91	
Intermediate risk	PFS	84	75	NA
	OS	92	79	
Poor risk	PFS	54	41	NA
	OS	73	48	
Testis cancer cohort	OS	94	NA	75

IGCCCG, International Germ Cell Cancer Collaborative Group; PFS, progression-free survival; OS, overall survival, NCI SEER: National Cancer Institute Surveillance, Epidemiology, and End Results Program.

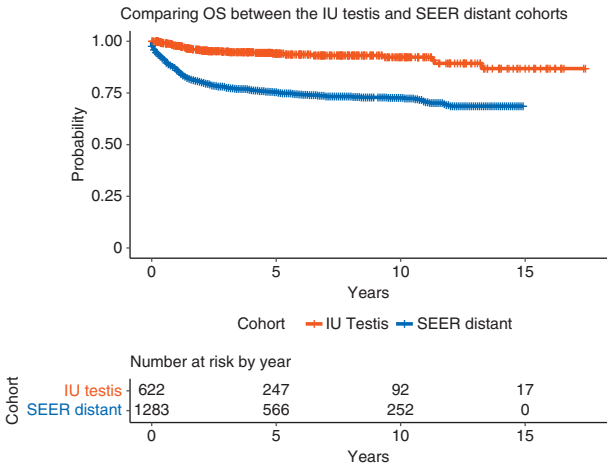

Figure 2. Kaplan–Meier estimates of overall survival of patients with newly diagnosed metastatic testicular GCT at the IU (1998–2014) and patients in NCI SEER (2000–2014).

Also, it could be attributed to the rare nature of this cancer and lack of experience in the community to establish an accurate diagnosis and deliver a treatment plan.

In conclusion, in this modern cohort of newly diagnosed metastatic GCT, there was an improvement in PFS and OS for good, intermediate, and poor-risk disease compared with IGCCCG. Furthermore, we demonstrated that a multidisciplinary team care approach is associated with improved survival outcomes compared with SEER distant cohort. Taken together, these data support reconstructing health delivery models to enhance value and improve clinical outcomes [9, 19].

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Disclosure

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References

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin 2017; 67: 7–30.
2. Williams SD, Birch R, Einhorn LH et al. Treatment of disseminated germ-cell tumors with cisplatin, bleomycin, and either vinblastine or etoposide. N Engl J Med 1987; 316(23): 1435–1440.
3. de Wit R, Roberts JT, Wilkinson PM et al. Equivalence of three or four cycles of bleomycin, etoposide, and cisplatin chemotherapy and of a 3- or 5-day schedule in good-prognosis germ cell cancer: a randomized study of the European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group and the Medical Research Council. J Clin Oncol 2001; 19(6): 1629–1640.
4. Einhorn LH, Williams SD, Loehrer PJ et al. Evaluation of optimal duration of chemotherapy in favorable-prognosis disseminated germ cell tumors: a Southeastern Cancer Study Group protocol. JCO 1989; 7: 387–391.
5. Culine S, Kerbrat P, Kramar A et al. Refining the optimal chemotherapy regimen for good-risk metastatic nonseminomatous germ-cell tumors: a randomized trial of the Genito-Urinary Group of the French Federation of Cancer Centers (GETUG T93BP). Ann Oncol 2007; 18(5): 917–924.
6. International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. J Clin Oncol 1997; 15: 594–603.
7. Collette L, Sylvester RJ, Stenning SP et al. Impact of the treating institution on survival of patients with "poor-prognosis" metastatic nonseminoma. European Organization for Research and Treatment of Cancer Genito-Urinary Tract Cancer Collaborative Group and the Medical Research Council Testicular Cancer Working Party. J Natl Cancer Inst 1999; 91(10): 839–846.
8. Nayan M, Jewett MA, Anson-Cartwright L et al. The association between institution at orchiectomy and outcomes on active surveillance for clinical stage I germ cell tumours. CUAJ 2016; 10: 204–209.
9. Jeldres C, Pham KN, Daneshmand S et al. Association of higher institutional volume with improved overall survival in clinical stage III testicular cancer: results from the National Cancer Data Base (1998–2011). JCO 2014; 32(4 Suppl): 4519–4519.
10. Adra N, Althouse SK, Liu H et al. Prognostic factors in patients with poor-risk germ-cell tumors: a retrospective analysis of the Indiana University experience from 1990 to 2014. Ann Oncol 2016; 27(5): 875–879.
11. Blanke C, Loehrer PJ, Nichols CR, Einhorn LH. A phase II trial of VP-16, ifosfamide, cisplatin, vinblastine, and bleomycin in advanced germ-cell tumors. Am J Clin Oncol 1996; 19(5): 487–491.
12. Motzer RJ, Nichols CJ, Margolin KA et al. Phase III randomized trial of conventional-dose chemotherapy with or without high-dose chemotherapy and autologous hematopoietic stem-cell rescue as first-line treatment for patients with poor-prognosis metastatic germ cell tumors. J Clin Oncol 2007; 25(3): 247–256.
13. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) Research Data (1973–2014), National Cancer Institute, DCCPS, Surveillance Research Program, released April 2017, based on the November 2016 Submission.
14. Gilligan TD, Seidenfeld J, Basch EM et al. American Society of Clinical Oncology Clinical Practice Guideline on uses of serum tumor markers in adult males with germ cell tumors. JCO 2010; 28: 3388–3404.

15. Necchi A, Pond GR, Nicolai N et al. A suggested prognostic reclassification of intermediate and poor-risk nonseminomatous germ cell tumors. Clin Genitourin Cancer 2017; 15(2): 306–312 e303.
16. Cary C, Pedrosa JA, Jacob J et al. Outcomes of postchemotherapy retroperitoneal lymph node dissection following high-dose chemotherapy with stem cell transplantation. Cancer 2015; 121(24): 4369–4375.
17. Albers P, Siener R, Krege S et al. Randomized phase III trial comparing retroperitoneal lymph node dissection with one course of bleomycin and etoposide plus cisplatin chemotherapy in the adjuvant treatment of clinical stage I nonseminomatous testicular germ cell tumors: AUO trial AH 01/94 by the German Testicular Cancer Study Group. JCO 2008; 26: 2966–2972.
18. Cho JS, Kaimakliotis HZ, Cary C et al. Modified retroperitoneal lymph node dissection for post-chemotherapy residual tumour: a long-term update. BJU Int 2017; 120(1): 104–108.
19. Tandstad T, Kollmannsberger CK, Roth BJ et al. Practice makes perfect: the rest of the story in testicular cancer as a model curable neoplasm. J Clin Oncol 2017; 35(31): 3525–3528.
20. Einhorn LH, Williams SD, Chamness A et al. High-dose chemotherapy and stem-cell rescue for metastatic germ-cell tumors. N Engl J Med 2007; 357(4): 340–348.
21. Feldman DR, Sheinfeld J, Bajorin DF et al. TI-CE high-dose chemotherapy for patients with previously treated germ cell tumors: results and prognostic factor analysis. J Clin Oncol 2010; 28(10): 1706–1713.
22. Kondagunta GV, Bacik J, Donadio A et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. J Clin Oncol 2005; 23(27): 6549–6555.
23. Loehrer PJ Sr, Einhorn LH, Williams SD. VP-16 plus ifosfamide plus cisplatin as salvage therapy in refractory germ cell cancer. J Clin Oncol 1986; 4(4): 528–536.
24. Loehrer PJ Sr, Gonin R, Nichols CR et al. Vinblastine plus ifosfamide plus cisplatin as initial salvage therapy in recurrent germ cell tumor. J Clin Oncol 1998; 16(7): 2500–2504.
25. Murphy BR, Breeden ES, Donohue JP et al. Surgical salvage of chemorefractory germ cell tumors. J Clin Oncol 1993; 11(2): 324–329.
26. Macleod LC, Cannon S, Ko O et al. Nationwide disparities in testicular cancer care delivery: racial, ethnic, and economic markers of patient vulnerability. JCO 2017; 35(6 Suppl): 421–421.
27. Sun M, Abdollah F, Liberman D et al. Racial disparities and socioeconomic status in men diagnosed with testicular germ cell tumors: a survival analysis. Cancer 2011; 117(18): 4277–4285.
28. Nichols CR, Jeldres C, Pham K et al. Influence of social demographics and African-American race on outcomes in testicular cancer: analysis of 75,902 patients in the National Cancer database. JCO 2014; 32(4 Suppl): 391–391.