original reports abstract

Low Survival in Poor Prognosis Metastatic Germ Cell Cancer in Belarus

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PURPOSE Since the development of the International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification in a 1997 study, high-income countries have reported a significant increase in survival for poor prognosis patients. There are scant data on IGCCCG risk-stratified survival from low- and middle-income countries. We assessed the progression-free survival (PFS) and overall survival (OS) rates in a contemporary cohort of Belarusian patients with advanced germ cell cancer (GCC) stratified by the IGCCCG prognostic classification and analyzed prognostic factors for survival.

MATERIALS AND METHODS The consecutive cohort of patients with clinical stage IIb-III testicular GCC or extragonadal germ cell tumors who received treatment or consultation in our two centers between 2010 and 2015 was included. All patients underwent primary chemotherapy. The patients were divided into seminoma and nonseminomatous germ cell carcinoma (NSGCC) subgroups. The Kaplan-Meier method was used to estimate 5-year PFS and OS.

RESULTS This study included 111 patients with a median age of 32 years, 95% of whom were diagnosed with testicular cancer. Seminoma and NSGCC were identified in 32 (29%) and 79 (71%) patients, respectively. The median follow-up was 6.1 years. The 5-year PFS and OS rates for the entire cohort were 70% and 77%, respectively. In patients with good prognosis seminoma and good, intermediate, and poor prognosis NSGCC, the estimated PFS rates were 76%, 88%, 74%, and 39% and those for OS were 83%, 97%, 83%, and 38%, respectively.

CONCLUSION In our cohort of Belarusian patients with advanced germ cell tumors, we failed to demonstrate an improvement in PFS and OS compared with the 1997 IGCCCG study. Moreover, survival in poor prognosis group is inferior to that in IGCCCG and all contemporary series from high-income countries.

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INTRODUCTION

Germ cell cancer (GCC) is one of the most common malignant neoplasms in young men.[1] Because of the rapid growth and aggressive course of the disease, some patients present in advanced stages and require primary systemic chemotherapy.[2] Because of late presentation issues, the proportion of patients with metastatic disease at diagnosis in low- and middle-income countries may be higher than in wealthy societies.[3] Thanks to the development of effective chemotherapy regimens—since the early 1980s, high cure rates have been achieved in patients with advanced GCC. However, the prognosis largely depends on a number of clinical factors, as found by the International Germ Cell Cancer Collaborative Group (IGCCCG) in a landmark 1997 study[4] with 5-year survival varying between 92% and 48%. Approaches to diagnosis, management, and delivery of care for these patients have since been improved, translating into increased long-term survival. Nevertheless, this increase has not been documented in low- and middle-income countries. Moreover, several epidemiological studies showed a marked increase in mortality or a decrease in the survival rate in patients with testicular cancer in Eastern European countries compared with the rest of Europe.[3,5]

The aim of the present study was to assess the survival rate in a contemporary cohort of Belarusian patients with advanced GCC stratified by the IGCCCG prognostic classification and to analyze prognostic factors for survival.

MATERIALS AND METHODS

Our study included the consecutive cohort of patients with clinical stage IIb-III testicular GCC or extragonadal germ cell tumors who received treatment or medical

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CONTEXT

Key Objective

To assess long-term oncologic outcomes stratified by the International Germ Cell Cancer Collaborative Group (IGCCCG) prognostic classification in a contemporary cohort of Belarusian patients with advanced germ cell cancer (GCC).

Knowledge Generated

Although we found satisfactory survival rate in good and intermediate prognostic groups, oncologic outcomes in poor prognosis GCC were inferior to those in the seminal 1997 IGCCCG study. This is contrary to data from high-income countries demonstrating significant survival improvement in the poor prognosis GCC and comparable results for patients with good and intermediate prognosis.

Relevance

Patients with poor prognosis advanced GCC are a particularly vulnerable subgroup of patients in Belarus demonstrating inferior survival compared with wealthier countries. These results may be responsible for the excess mortality in patients with testicular cancer from low- and middle-income countries. Continued effort is required to improve the quality of management of poor prognosis patients with advanced GCC in our country.

consultation in our two centers between 2010 and 2015. Histological confirmation of GCC was not required provided patients had a typical presentation of the disease with high level of serum tumor markers. All patients received primary chemotherapy. We excluded patients who had undergone primary retroperitoneal lymph node dissection (n = 14) or retroperitoneal radiotherapy (n = 8) and one patient without data on treatment and follow-up.

Information on the histological structure of the tumor, tumor stage, localization of metastases, and prechemotherapy tumor marker levels after inguinal orchiectomy was obtained from medical records. In the absence of these data, we used preorchiectomy marker levels. Depending on tumor burden and marker levels, the T, N, M, and S categories were determined in accordance with the Union for International Cancer Control (UICC) classification (7th edition, 2011). We divided all patients into two subgroups by tumor histology and tumor marker levels: pure seminoma and nonseminomatous germ cell carcinoma (NSGCC). The latter also included patients with pure seminoma histology and abnormal serum alpha-fetoprotein or high (> 1,000 mIU/mL) beta subunit of human chorionic gonadotropin levels. All patients were assigned a prognostic group according to the IGCCCG classification.[4] Additionally, we selected information on treatment: regimen and number of first-line chemotherapy cycles, surgery, and/or radiotherapy for residual tumor after chemotherapy.

The data on patients' survival status at the end of 2019 were retrieved from the Belarusian Cancer Registry. Progression-free survival (PFS) was defined as the interval from orchiectomy, or tumor biopsy, or the start of chemotherapy when histological verification was not performed to date of progression, death from any cause, or the end of observation, or loss of follow-up, whichever occurred first. The end of overall survival (OS) interval was death from any cause, end of observation, or loss of follow-up. Survival was calculated using the Kaplan-Meier method. The statistical significance for differences was assessed with the log-rank test. The risks of death and their 95% confidence intervals depending on factors included were assessed using Cox proportional hazards analysis. All *P* values were two-sided; $P < .05$ was considered as statistically significant. Statistical analyses were performed with R version 4.0.2 (The R Foundation for Statistical Computing, License GNU GPL v2).

RESULTS

A total of 111 patients from 14 to 76 years of age (median age of 32 years) were included in this study, of whom 106 (95%) were diagnosed with testicular cancer, four with extragonadal tumors of the retroperitoneum, and one with mediastinal tumor. Of the 106 patients with testicular cancer, four underwent scrotal violation and another 13 underwent biopsies of metastases before consulting a urologist, suggesting difficulty in identifying primary tumors. Three patients received urgent chemotherapy without any attempt to histologically verify the disease (n = 2) or without clear histological verification of NSGCC with the biopsy of metastases (n = 1). In one of these patients, after completion of chemotherapy in the testis, ypT2 teratoma was verified. The remaining two patients had a clinical picture and high levels of tumor markers typical for NSGCC.

Overall, clinically and histologically pure seminoma was identified in 32 (29%) patients, of whom 30 (94%) had a good prognosis according to IGCCCG and two (6%) had an intermediate one because of the presence of extrapulmonary visceral metastases. Seventy-nine (71%) patients were diagnosed with NSGCC, of whom 30 (38%), 24 (30%), and 18 (23%) patients had good, intermediate, and poor prognosis, respectively. In seven patients (9%), the prognostic group was not established because of the lack of data on prechemotherapy tumor marker levels. Patient characteristics are presented in Table 1.

TABLE 1. Patients Characteristics

Variable	Total	Seminoma	NSGCC	*P*
Primary				
Testis	106 (95)	30 (94)	76 (96)	.29
Right	63 (57)[a]	16 (50)[a]	47 (59)	
Left	44 (40)[a]	15 (47)[a]	29 (37)	
Extragonadal	5 (5)	2 (6)	3 (4)	
Age				
Median (IQR)	32 (26-40)	42 (37-48)	29 (34-35)	
< 35 years	65 (59)	6 (19)	59 (75)	< .001
≥ 35 years	46 (41)	26 (81)	20 (25)	
Predominant histology				
Seminoma	38 (34)	32 (100)	6 (8)[b]	< .001
Mixed tumors	38 (34)	0	38 (48)	
Embryonal	23 (21)	0	23 (29)	
Teratoma	4 (4)	0	4 (5)	
Yolk sac tumor	4 (4)	0	4 (5)	
Choriocarcinoma	2 (2)	0	2 (3)	
No data	2 (2)	0	2 (3)	
T stage[c]				
Tx/ypT0/ypT2	2/5/1 (7)[a]	0/3/0 (9)[a]	2/2/1 (6)	.7
pT1	13 (12)[a]	3 (9)[a]	10 (13)	
pT2	62 (56)[a]	20 (63)[a]	42 (53)	
pT3-4	24 (22)[a]	5 (16)[a]	19 (24)	
N stage[c]				
N0	5 (5)	0	5 (6)	.002
N1	3 (3)	0	3 (4)	
N2	48 (43)	7 (22)	41 (52)	
N3	50 (45)	23 (72)	27 (34)	
M stage[c]				
M0	40 (36)	17 (53)	23 (29)	.04
M1a	54 (49)	11 (34)	43 (54)	
M1b	12 (11)	2 (6)	10 (13)	
S category				
S0-1	56 (50)	25 (78)	31 (39)	< .001
S2	27 (24)	0	27 (34)	
S3	11 (10)	0	11 (14)	
No data	17 (15)	7 (22)	10 (13)	
Clinical stage[c]				
IIb	23 (21)	4 (13)	19 (24)	< .001
IIc	17 (15)	13 (41)	4 (5)	
III	66 (59)	13 (41)	53 (67)	
IGCCCG prognosis group				
Good	60 (54)	30 (94)	30 (38)	< .001
Intermediate	26 (23)	2 (6)	24 (30)	
Poor	18 (16)	0	18 (23)	
No data	7 (6)	0	7 (9)	

(Continued on following page)

TABLE 1. Patients Characteristics (Continued)

Variable	Total	Seminoma	NSGCC	*P*
Treatment				
Chemotherapy				
BEP	58 (52)	18 (56)	40 (51)	.89
EP	7 (6)	3 (9)	4 (5)	
VIP or VeIP	3 (3)	1 (3)	2 (3)	
BEP + EP	32 (29)	7 (22)	25 (32)	
BEP + VIP or TIP	8 (7)	2 (6)	6 (8)	
Other	3 (3)	1 (3)	2 (3)	
Number of cycles				
< 3 cycles	11 (10)	4 (13)	7 (9)	.79
3 cycles	20 (18)	7 (22)	13 (16)	
4 cycles	43 (39)	12 (38)	31 (39)	
> 4 cycles	37 (33)	9 (28)	28 (35)	
Surgery				
Yes	52 (47)	3 (9)	49 (62)	< .001
No	59 (53)	29 (91)	30 (38)	
Radiotherapy				
Yes	15 (14)	12 (38)	3 (4)	< .001
No	96 (86)	20 (63)	76 (96)	

Abbreviations: BEP, bleomycin, etoposide, and cisplatin; EP, etoposide and cisplatin; IGCCCG, International Germ Cell Cancer Collaborative Group; IQR, interquartile range; NSGCC, nonseminomatous germ cell cancer; TIP, paclitaxel, ifosfamide, and cisplatin; VeIP, vinblastine, ifosfamide, and cisplatin; VIP, etoposide, ifosfamide, and cisplatin;

[a]The sum exceeds 100% as one patient had synchronous bilateral seminoma.

[b]With clinical signs of NSGCC.

[c]Excluding extragonadal tumors.

Patients received one to nine cycles of first-line chemotherapy (median number of cycles is four). Fewer than three cycles were given to 11 (10%) patients generally because of early death or treatment refusal. Thirty-eight (35%) patients received a full course of chemotherapy outside our centers, and in another 23 patients (21%), total chemotherapy course was split between our centers and local oncology clinics. Postchemotherapy surgery for residual tumor was performed in 49 (62%) patients with NSGCC and three (9%) patients with seminoma. Twelve (38%) patients with seminoma and three (4%) patients with NSGCC received consolidation radiotherapy.

The median follow-up was 6.1 years. During this period, 33 (30%) events of PFS occurred and 26 (23%) patients died. The 5-year PFS and OS for the entire cohort were 70% and 77%, respectively. Patients with seminoma and NSGCC showed the 5-year PFS rates of 78% and 66% (P = .30) and OS rates of 84% and 74% (P = .32), respectively. In good prognosis, the PFS and OS of patients with seminoma were 76% and 83%, respectively. The survival rate for two patients with intermediate prognosis was not calculated. In patients with NSGCC in good, intermediate, and poor prognosis groups, the 5-year PFS estimates were 88%, 74%, and 39% (P < .001, Figure 1) and the OS rates were 97%, 83%, and 38% (P < .001), respectively (Figure 2).

Of note, of 10 men with poor prognosis NSGCC because of the presence of extrapulmonary visceral metastases, eight (80%) patients died compared with three of eight (38%) included in the poor prognosis group only because of high tumor marker levels (S3). The 3-year OS rates in these two subgroups were 20% and 88% (P = .018), respectively.

The results of the univariate Cox proportional hazards analysis for OS are shown in Table 2. In the pure seminoma subgroup, retroperitoneal lymph node dissection was statistically significantly associated with an increased risk of death. In patients with NSGCC, statistically significant adverse factors for OS were age older than 35 years, extragonadal localization of the primary tumor, presence of distant and, particularly, extrapulmonary visceral metastases, increase in S category, IGCCCG prognostic group, fewer than three cycles of induction chemotherapy, lack of postchemotherapy surgery, and presence of consolidation radiotherapy for residual metastases.

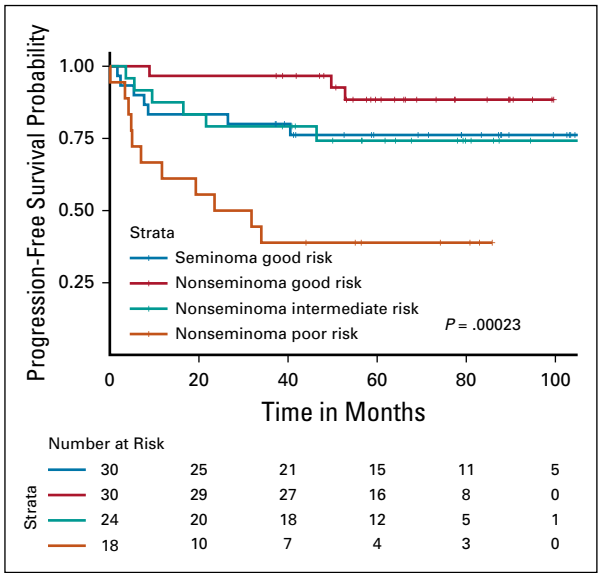

FIG 1. Progression-free survival of patients according to the International Germ Cell Consensus Classification and pathology.

DISCUSSION

Advanced germ cell tumors have long been known to be a heterogeneous group with widely varying prognosis. This led to the development of several prognostic classifications by individual high-volume centers.[6,7] Subsequently, the core prognostic criteria for stratifying patients into groups with different prognoses were developed and validated in a large cooperative study that combined patients from 10 countries.[4] Researchers from the IGCCCG analyzed the data of 5,202 patients with NSGCC and 660 patients with seminoma with a 5-year follow-up. For NSGCC, the independent adverse factors were mediastinal primary site, degree of elevation of tumor marker levels, and presence of nonpulmonary visceral metastases. For seminoma, the only adverse feature was the presence of nonpulmonary visceral metastases. Integration of these factors produced three risk groups with good, intermediate, and poor prognosis, in which the 5-year OS rates were 91%, 79%, and 48%, respectively. These became the reference data for evaluating treatment outcomes in the subsequent series.

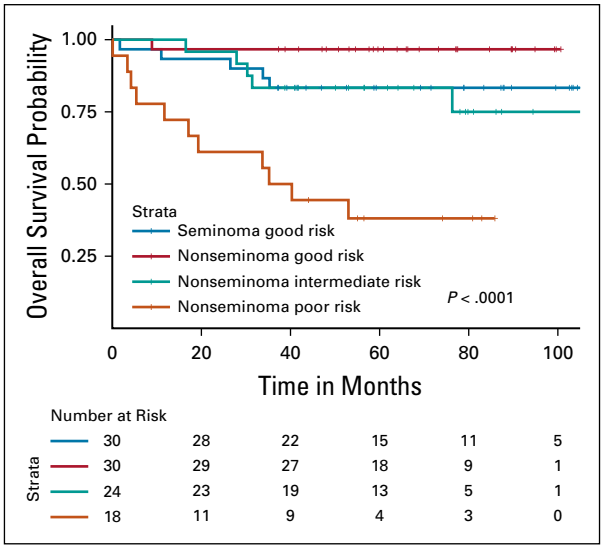

FIG 2. Overall survival of patients according to the International Germ Cell Consensus Classification and pathology.

A number of studies published after 2000 confirmed the high predictive ability of the IGCCCG classification and showed a gradual improvement in patient outcomes (Table 3).[8-13] All these studies came from high-income countries and demonstrated a significant improvement in 5-year OS in the poor prognosis group from 48% to 60%-73% and comparable data or a slight improvement in survival rates (except for the last study[13]) for patients with good and intermediate prognosis. On the contrary, our study demonstrated a significantly lower OS in the poor prognosis group (38%) even when compared with historical data.[4] The groups with good and intermediate prognosis showed results comparable with those in the above studies except, possibly, patients with good prognosis seminoma.

There are scant data on IGCCCG risk-specific treatment results in low- or middle-income countries. We found only two publications from highly specialized tertiary referral centers in India[14] and Brazil,[15] which showed results comparable with the previously cited studies. In contrast to the last two publications, we showed a broader perspective of GCC outcomes in Belarus. Although all patients were seen at two tertiary cancer centers, 55% of patients received a full or partial chemotherapy course outside of our clinics, making our study more representative of routine clinical practice in the country. The weakness of our study is the lack of countrywide data. Unfortunately, we were not able to use the national cancer registry since it provides no information on tumor markers and risk groups. However, the accuracy of clinical information in the cancer registry is clearly lower than that in the analysis of primary records in our centers.

Late diagnosis, severe complications of the disease, poor performance status, compliance issues, treatment toxicity, quality of therapy, and adherence to treatment guidelines could be responsible for inferior survival in our poor prognosis patients. There is evidence that at least some of these causes have affected treatment outcomes in the present study. In our total cohort, 16% of patients with testicular cancer either underwent either scrotal violations or biopsy of metastases in the presence of a detectable testicular tumor. The poor prognosis group included 24% of such patients, providing potential for delayed diagnosis and treatment. A significant number of poor prognosis patients were detected in a severely symptomatic stage with decreased performance, which caused high mortality during treatment: for example, three (17%) of four patients who received fewer than three cycles of chemotherapy died during the treatment. Of 11 (10%) patients from the total cohort with an insufficient (< 3) number of chemotherapy

TABLE 2. Results of Univariate Cox Proportional Hazards Regression Analysis

	Total Cohort		Seminoma		NSGCC	
Variables	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Age: ≥ 35 *v* < 35 years	1.89 (0.87 to 4.09)	.11	1.00 (0.11 to 8.98)	1.0	3.58 (1.51 to 8.47)	.004
Age: 10-year increase	1.42 (0.97 to 2.09)	.075	1.84 (0.61 to 5.54)	.28	2.11 (1.31 to 3.39)	.002
NSGCC *v* seminomatous	1.80 (0.68 to 4.77)	.24	—	—	—	—
Extragonadal *v* gonadal	5.93 (2.02 to 17.4)	.001	5.26 (0.58 to 47.9)	.14	7.13 (2.06 to 24.7)	.002
Category M1 *v* M0	4.39 (1.30 to 14.9)	.017	1.28 (0.18 to 9.09)	.81	8.93 (1.19 to 67.1)	.033
Extrapulmonary visceral metastases *v* other distant	6.46 (2.78 to 15.0)	< .001	0.04 (0 to 246,911)	.70	9.69 (3.88 to 24.2)	< .001
Clinical stage IIc-III *v* IIb	30.9 (0.47 to 2,017)	.11	25.4 (0 to 5,450,800)	.61	34.1 (0.44 to 2,627)	.112
S category	—	.010	—	—	—	.031
S2 *v* S0-1	2.18 (0.76 to 6.22)	.15	—	—	2.12 (0.62 to 7.25)	.23
S3 *v* S0-	5.42 (1.82 to 16.2)	.002	—	—	5.31 (1.50 to 18.8)	.010
IGCCCG risk group	—	< .001	—	—	—	.001
Intermediate *v* good	1.94 (0.59 to 6.36)	.27	0.04 (0 to 246,911)	.70	6.51 (0.76 to 55.7)	.087
Poor *v* good	8.65 (3.19 to 23.5)	< .001	—	—	26.8 (3.45 to 208)	.002
Number of chemotherapy cycles	—	< .001	—	.12	—	< .001
> 4 *v* 3-4	1.87 (0.74 to 4.71)	.19	1.12 (0.10 to 12.4)	.92	2.00 (0.73 to 5.52)	.18
< 3 *v* 3-4	10.1 (3.89 to 26.4)	< .001	6.92 (0.96 to 49.8)	.055	13.8 (4.56 to 41.4)	< .001
Surgery *v* no surgery	0.35 (0.15 to 0.84)	.018	6.53 (1.09 to 39.3)	.040	0.14 (0.05 to 0.38)	< .001
Radiotherapy *v* no radiotherapy	0.80 (0.24 to 2.67)	.72	0.37 (0.04 to 3.34)	.38	4.72 (1.09 to 20.5)	.038

Abbreviations: HR, hazard ratio; IGCCCG, International Germ Cell Cancer Collaborative Group; NSGCC, nonseminomatous germ cell cancer.

cycles, six did not finish treatment probably because of noncompliance and one patient stopped chemotherapy because of cardiac complication.

The quality of therapy may be another issue in this subgroup of patients. Although we did not assess the relative dose intensity of chemotherapy, the number of chemotherapy cycles either met the guidelines (28% of patients received four cycles) or exceeded them (50% of patients received more than four cycles). Eight (44%) patients underwent surgery to remove residual lesions in the retroperitoneum and/or chest, and two (11%) patients received consolidation radiotherapy for residual tumor in the brain or bone. By comparison, the frequency of postchemotherapy surgery for NSGCC in the previously cited studies ranged from 36%[11] to 75%.[10] In published phase III studies with poor prognosis patients, the incidence of postchemotherapy surgery varied from 63% to 86%.[16,17]

The analysis of prognostic factors showed different results for patients with seminoma and NSGCC: in patients with pure seminoma, statistically significant prognostic factors were not identified, and in NSGCC patients of age older than 35 years, extragonadal site of the primary tumor, presence of distant metastases, extrapulmonary visceral metastases, and increase in S category statistically significantly worsened the prognosis. The majority of these factors are components of the IGCCCG prognostic classification, which confirms its high prognostic significance. We also confirm other authors' observations that age could significantly affect prognosis, which may be explained by an increase in tumor resistance to chemotherapy or a decrease in the patient's tolerance to toxic therapy.[18,19]

It is no surprise that the results of germ cell cancer treatment in our study are worse than those are in report series from Japan, Northern Europe, and the United States since epidemiological studies provide ample evidence of higher mortality and lower survival rates for patients with testicular cancer in less wealthy countries, particularly in Eastern Europe.[3,5,20] Nevertheless, our research may shed some light on the reasons for these differences. Our results suggest that the most vulnerable cohort of patients, apparently responsible for the decline in overall outcomes, is the poor prognosis group. We could speculate that in this most difficult group of patients, where not only coordinated efforts of multidisciplinary medical teams but also the help of patients' families with logistics and support are required, systemic problems of care delivery for patients with cancer and unfavorable social factors (including low income, residence in rural areas, long distance from the cancer care provider, etc) may be apparent and significantly affect survival.

In conclusion, in our cohort of Belarusian patients with advanced germ cell tumors, we failed to demonstrate an improvement in PFS and OS compared with the 1997 IGCCCG study. Moreover, survival in the poor prognosis group is inferior to that in IGCCCG and all contemporary series from high-income countries.

TABLE 3. Comparison of Published Survival Estimates in Patients With Metastatic Germ Cell Cancer With Stratification by International Germ Cell Cancer Collaborative Group Prognostic Classification

First Author, Year of Publication	Study Settings and Patients' Cohort Characteristics	Study Period	No. of Patients	5-Year PFS, %			5-Year OS, %		
				Good Prognosis	Intermediate Prognosis	Poor Prognosis	Good Prognosis	Inter-mediate Prognosis	Poor Prognosis
Mead et al, 1997[4]	Pooled analysis of data on patients with mGCC from 10 countries treated with cisplatin-containing chemotherapy	1975-1990	5,202 (NS) 660 (S)	89 (NS) 81 (S)	75 (NS) 67 (S)	41 (NS)	92 (NS) 85 (S)	80 (NS) 72 (S)	48 (NS)
van Dijk et al, 2006[8]	Meta-analysis of 10 studies (phase II-III and hospital registries) reporting survival of patients with mNSGCC	1989-2001	1,775 (NS)	NR	NR	NR	94 (NS)	83 (NS)	71 (NS)
Shintaku et al, 2008[9]	Pooled analysis of data on patients with mGCC treated at seven hospitals in Japan	1990-2001	227 (NS) 69 (S)	96 (NS) 78 (S)	71 (NS) 80 (S)	52 (NS)	94 (NS) 90 (S)	81 (NS) 80 (S)	61 (NS)
Olofsson et al, 2011[10]	Long-term results of prospective population-based study on treatment of mNSGCC by Swedish-Norwegian Testicular Cancer Group	1995-2003	603 (NS)	87 (NS)[a]	85 (NS)[a]	64 (NS)[a]	95 (NS)[a]	90 (NS)[a]	67 (NS)[a]
Kier et al, 2017[11]	Analysis of Danish population-based cohort of patients with mGCC after first-line BEP chemotherapy	1984-2007	1,469 (NS) 420 (S)	90 (NS) 87 (S)	76 (NS)	55 (NS)	95 (NS) 93 (S)	85 (NS)	64 (NS)
Albany et al, 2018[12]	Single-center data on mGCC patients started first-line chemotherapy at Indiana University (USA)	1998-2014	598 (NS) 106 (S)	90 (NS + S)	84 (NS + S)	54 (NS)	97 (NS + S)	92 (NS + S)	73 (NS)
Mazzone et al, 2019[13]	Analysis of data from population-based SEER database (USA) on patients with metastatic testis cancer	2004-2015	803 (NS) 319 (S)	NR	NR	NR	89 (NS) 87 (S)	75 (NS) 78 (S)	60 (NS)
Saju et al, 2019[14]	Single-center data on patients with GCC treated at Adyar Cancer Institute, Chennai (India)	2001-2015	254 (NS) 83 (S)	76 (NS)[b] 81 (S)[b]	73 (NS)[b] 78 (S)[b]	41 (NS)[b]	83 (NS)[b] 89 (S)[b]	82 (NS)[b] 81 (S)[b]	52 (NS)[b]
Vasconcellos et al, 2019[15]	Single-center data on patients with mGCC treated at Instituto do Cancer do Estado de São Paulo (Brazil)	2000-2015	136 (NS) 95 (S)	83 (NS + S)	71 (NS + S)	35 (NS)	95 (NS + S)	84 (NS + S)	62 (NS)
Present study, 2020	Analysis of patients with mGCC treated at different oncological clinics in Belarus	2010-2015	79 (NS) 32 (S)	88 (NS) 76 (S)	74 (NS)	39 (NS)	97 (NS) 83 (S)	83 (NS)	38 (NS)

Abbreviations: (m)GCC, (metastatic) germ cell cancer; mNSGCC, metastatic nonseminomatous germ cell cancer; NR, not reported; NS, nonseminoma; OS, overall survival; PFS, progression-free survival; S, seminoma.

[a]10-year estimates.

[b]3-year estimates.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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