The Value of Centers of Excellence:

Patients with relapsed testicular cancer benefit from salvage therapy provided through multidisciplinary care

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The largest, single-institution retrospective analysis of patients with metastatic germ-cell cancer treated with salvage chemotherapy highlighted effective treatment methods and the benefit of patients receiving multidisciplinary care from centers of testicular cancer excellence, such as the Indiana University Health Medical Center.

Overview

Germ-cell tumors are the most common cancer in men between 15 and 35 years of age, and patients with metastatic disease are curable. While patients with anatomically confined disease who relapse after initial chemotherapy can still be cured by undergoing salvage surgery, the vast majority of patients will be treated with salvage chemotherapy. While the most effective regimen for these patients is still debated, at IU Health Medical Center we know that treating these patients with this regimen is successful.

Our research team set out to answer that question. Our study in the *Journal of Clinical Oncology* included a retrospective analysis that studied 364 consecutive patients (316 with primary tumor site in the testis) whose germ-cell tumors (GCT) had progressed after cisplatin-based combination chemotherapy was followed by subsequent treatment with high-dose chemotherapy (HDCT) and peripheral-blood stem-cell transplantation (PBSCT). Through the largest single-institution study evaluating HDCT in patients with relapsed GCT, our findings indicate that these patients are curable by HDCT plus PBSCT, even when used in third-line or later therapy. This course of treatment was first investigated at Indiana University in 1986 using bone marrow transplantation. The combination of HDCT and PBSCT, as our study showed, has proven to be an effective offering in our multidisciplinary care at a center of testicular cancer excellence at IU Health Medical Center. In fact, we find most first recurrences of testicular cancer now have the potential for cure.

Patients & Methods

The patients we reviewed were treated with HDCT and PBSCT at IU Health Medical Center between 2004 and 2014.

- The median age was 32 years (ranging between 17 to 70 years)
- The primary tumor site was testis in 316 patients, retroperitoneum in 28 patients and mediastinum in 20 patients
- Initial IGCCCG criteria (International Germ Cell Cancer Collaborative Group) classified patients' risk criteria as 151 good risk, 39 intermediate risk and 174 poor risk
- 341 patients received two consecutive courses of HDCT consisting of 700 mg/m2 carboplatin and 750 mg/m2 etoposide
  - Each for three consecutive days and
  - Each followed by PBSCT
- 23 patients received only a single course of HDCT because of progressive disease or toxicity

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Findings

This large, single-institution study demonstrates that patients with relapsed metastatic GCT are curable by HDCT plus PBSCT, even when used in third-line or later therapy. With a median follow-up of 3.3 years, the two-year progression-free survival (PFS) was 60%, and the two-year overall survival was 66%.

Although this study included a high proportion of patients with poor prognostic factors at initiation of HDCT, survival outcomes still appeared better compared to previous studies that evaluated standard-dose salvage chemotherapy. Our research suggests that high-dose chemotherapy and peripheral-blood stem-cell transplant is effective salvage therapy for patients with relapsed GCT, delineating remarkable chemosensitivity of this disease.

Characteristic	No. of Patients (N = 364)	%
Median age, years (range)	32 (17-70)	
Location of primary tumor		
Testis	316	87
Retroperitoneum	28	8
Mediastinum	20	5
Tumor histology		
Seminoma	79	22
Nonseminoma	285	78
Metastatic site(s)		
Retroperitoneum	281	77
Pulmonary	217	60
NPVM	122	34
Liver	75	21
Brain*	64	18
Bone*	25	7
Brain metastasis		
None	300	82
Inactive/previously treated	44	12
Progressive	20	6
Initial IGCCCG risk		
Good	151	41
Intermediate	39	11
Poor	174	48
Progression-free interval after first-line chemotherapy, weeks		
< 4	118	32
4-12	54	15
> 12	192	53
Platinum sensitivity		
Sensitive	242	66
Refractory	122	34
No. of previous chemotherapy regimens		
1	303	83
2	55	15
≥ 3	6	2
Median serum AFP ng/mL (range)	7.5 ng/mL (1-21,347)	
Serum AFP level < 1,000	336	92
Serum AFP level ≥ 1,000	28	8
Median serum hCG mIU/mL (range)	37.1 mIU/mL (0.5-178,140)	
Serum hCG < 1,000	274	75
Serum hCG ≥ 1,000	90	25
ECOG performance status		
0	305	84
1	37	10
2	22	6
Risk per IPFSG criteria (N = 303)		
Very low	34	11
Low	55	18
Intermediate	77	25.5
High	77	25.5
Very high	60	20

Abbreviations: AFP, alpha-fetoprotein; ECOG, Eastern Cooperative Oncology Group; hCG, human chorionic gonadotropin; IGCCCG, International Germ Cell Cancer Collaborative Group; IPFSG, International Prognostic Factors Study Group; NPVM, nonpulmonary visceral metastasis.
*Brain/bone imaging was not mandatory.

Table 1. *Patient and Disease Characteristics at the Beginning of High-Dose Chemotherapy*

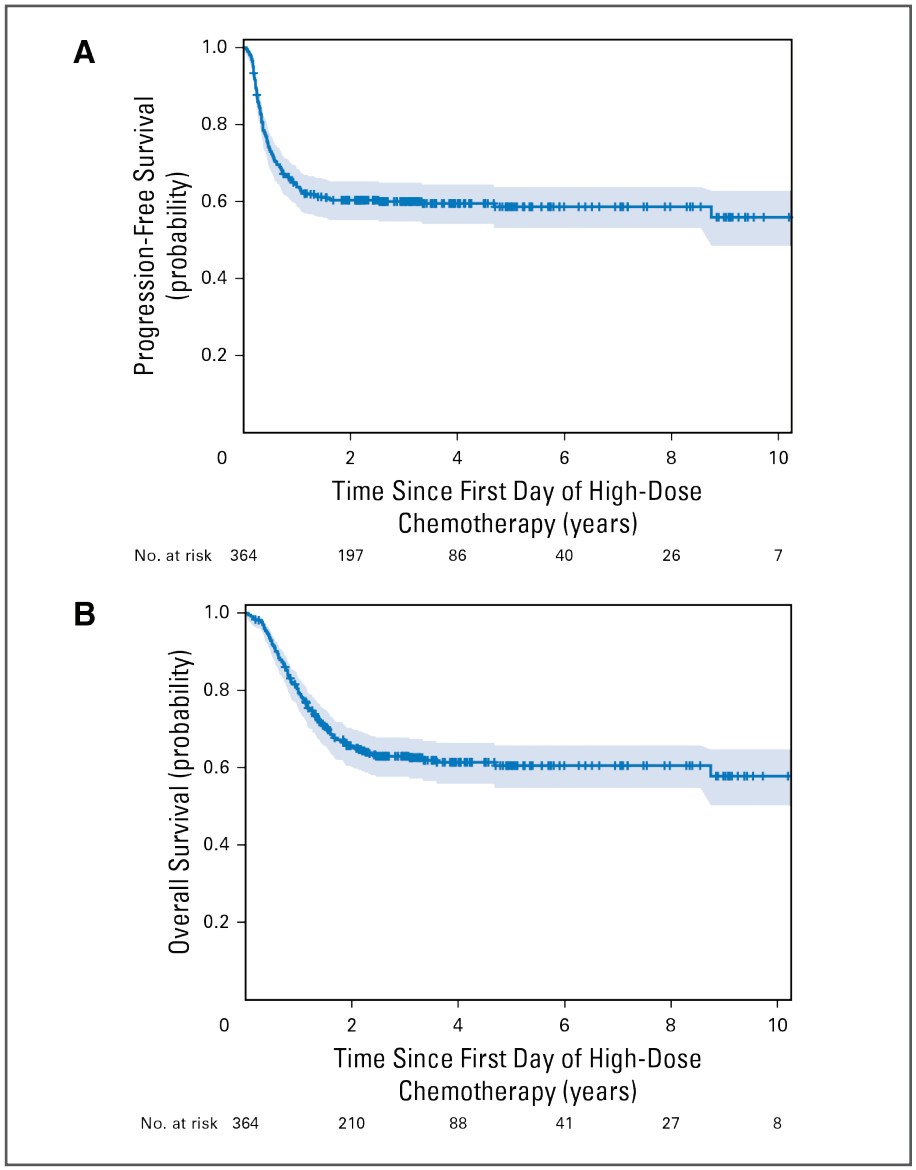

Figure 1. Kaplan-Meier estimates of (A) progression-free survival and (B) overall survival for 364 patients

Discussion

While this study included a large sample size of consecutive patients and lengthy follow-up, it is limited to this type of setting: a testicular cancer center of excellence. Patients in this study were treated at IU Health Medical Center: an experienced, high-volume referral center for metastatic GCT where the revolutionary cisplatin-based front-line combination chemotherapy was first developed 45 years ago. Survival outcomes for patients treated at other institutions may vary. It is our opinion that **these patients require multidisciplinary expertise and should be cared for at centers of testicular cancer excellence.**

IU Health is at the leading edge of expert testicular cancer care. We're ready to partner with you.

Contact IU Health

Have an immediate referral or want to consult with our team? Call our urological oncologists at 317.944.0920.