Outcome of germ cell tumour patients treated with high-dose chemotherapy in the UK: a 20-year retrospective review of the BSBMTCT database

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BACKGROUND

- High-dose chemotherapy with stem cell transplant (HDCT/SCT) is a treatment option in patients with recurrent germ cell tumour (GCT).
- The British Society of Blood and Bone Marrow Transplantation and Cellular Therapy (BSBMTCT) is an organisation for health care professionals with an interest in haematopoietic cell transplantation and cellular therapies.
- The BSBMTCT established a SCT registry in 2001 to monitor outcomes of patients treated within the UK and Republic of Ireland. Data reporting is now necessary for centre accreditation. Of note, this registry also includes historical data from before 2001.
- We performed a retrospective analysis of the registry to evaluate outcomes of HDCT/SCT in GCT patients treated from 01/01/2000 to 31/12/2019.

METHODS

- Written consent were obtained from patients at the time of SCT for data to be collected and held in the registry and used for research and service evaluation purposes. The study protocol was approved by the BSBMTCT Clinical Trials Committee.
- Standard data forms were used to collect patient data. Data was collected at registration, 100 days post transplant, and annually thereafter.
- Data entry was performed at each site by a data manager. Of note, most data entry was performed by the haematology team supporting the SCT procedure rather than by germ cell oncologists.

RESULTS

- Data from 671 transplants in 467 patients across 24 centres were included. 42% of patients were included in the period 2000-09; 58% from 2010-2019.
- The median time from initial GCT diagnosis to first transplantation was 1.25years (y), range 0.17-38y.
- Most patients were fit young males with primary gonadal non-seminomatous GCT. The registry also included a cohort of female patients and a small cohort of paediatric patients. A summary of the key data is shown in tables A-E. Data fields reported as other/unknown were frequent.
- Of the 75 female patients, 30 (40%) had histology reported as choriocarcinoma (1 patient aged <16y; 29 aged ≥16y). These patients potentially reflect those with gestational trophoblastic disease (GTD). All 30 were transplanted at the two GTD treatment centres. Interestingly, the survival outcomes in these patients were similar to the patients with non-choriocarcinoma/GTD histology (Figure 4)
- 16/30 (53%) of the paediatric patients had primary CNS disease, and 16/27 (59%) of the patients with primary CNS disease were paediatric; the oldest patient with primary CNS disease was 33y. Histology for patients with primary CNS disease was poorly reported with most (67%) being unknown.
- Across all patients, the 10y survival was 39% (95%CI: 34-44%) with most deaths occurring in the first 2y (Figure 1). Survival outcomes across different time periods were similar (Figure 2).
- At 100 days, 117 patients (25%) were alive and in complete remission, 230 (49%) alive but not in complete remission, 80 (17%) alive but relapsed, 20 (4%) had died due to relapse and 20 (4%) died due to treatment-related causes. As shown in Figure 8, non-relapse related mortality was relatively stable after the first 6 months.
- Patients reported to have chemoresistent disease at the time of transplant had significantly worse survival outcomes than patients with chemosensitive disease (Overall survival (OS) at 10y resistant vs sensitive disease: 18% (95%CI: 9-29) vs 50% (95%CI: 40-54); p<0.001; Figure 7).

CONCLUSIONS

- This study reports real-world outcomes from HDCT/SCT in a large contemporary cohort of GCT patients.
- Survival outcomes appeared stable over time with two-fifths of patients alive at 10 years.
- Survival outcomes in male and female patients aged ≥16y were similar.
- Of note, only 10% of patients were reported to have been treated within a clinical trial, representing a missed opportunity to progress treatments.
- Closer working between GCT oncologists, haematologists and the BSBMTCT would improve the quality of the GCT data recorded and potentially allow for use of the registry to examine other aspects of care such as the late effects of HDCT.
- Of note, this study is not able to examine the merits of conventional dose vs HDCT in relapsed GCT. Results from the international TIGER study (NCT02375204) are eagerly awaited.

ACKNOWLEDGEMENTS

- We thank all the patients and involved treating centres for collecting and contributing data to this study.

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TABLES

Tables summarising key clinical data are shown. Table A shows data for the whole study cohort; B male patients aged ≥16y; C female patients aged ≥16y; D paediatric patients (aged <16y); and E patients with primary CNS disease.

A

All patients		N = 467
Year of first transplant	2000-2004 2005-2009 2010-2014 2015-2019	97 (21%) 101 (21%) 134 (29%) 135 (29%)
Patient sex	Male Female	392 (84%) 75 (16%)
Age at diagnosis (y)	<16 ≥16 Median (range)	30 (7%) 437 (93%) 29 (0.5-66y)
Number of transplants per patient	1 2 3	305 (65%) 120 (26%) 42 (9%)
Karnofsky/Lansky status at first transplant	100-90 50-80 Unknown	281 (60%) 63 (13%) 123 (26%)
Comorbidity at first transplant	Yes No Unknown	167 (36%) 122 (26%) 178 (38%)
Distant metastases at first transplant	Yes No Unknown	153 (33%) 75 (16%) 239 (51%)
Prognostic risk category at first transplant	Very high High Intermediate Low Very low Unknown	31 (7%) 72 (15%) 39 (8%) 14 (3%) 3 (1%) 308 (66%)
Disease status at first transplant	Complete remission Partial remission Stable disease Progressive disease Unknown	66 (14%) 148 (32%) 59 (13%) 18 (4%) 176 (38%)
Chemosensitivity	Sensitive Resistant Unknown	252 (54%) 58 (12%) 157 (34%)
Conditioning regimen	Carboplatin/Etoposide Carboplatin/Cyclophosphamide/Etoposide Carboplatin/Cyclophosphamide/Etoposide/ Paclitaxel Carboplatin/Thiotepa/Topotecan Other carboplatin-based regimen Other non-carboplatin regimen Unknown	117 (25%) 53 (11%) 117 (25%) 63 (13%) 40 (9%) 20 (4%) 57 (12%)
Patient in clinical study	Yes No Unknown	46 (10%) 392 (84%) 29 (6%)

B

Male patients aged ≥16y		N = 372
Primary tumour site	Gonadal Retroperitoneal Mediastinal CNS Other/unknown	274 (74%) 21 (6%) 33 (9%) 10 (3%) 34 (9%)
Histology	Seminoma Non-seminoma Unknown	62 (17%) 289 (78%) 21 (6%)

C

Female patients aged ≥16y		N = 65
Primary tumour site	Gonadal Retroperitoneal Mediastinal CNS Other/unknown	61 (94%) 0 (0%) 2 (3%) 1 (2%) 1 (2%)
Histology	Seminoma Non-seminoma Choriocarcinoma/GTD* Unknown	1 (2%) 61 (94%) 29 3 (5%)

*Choriocarcinoma potentially reflecting gestational trophoblastic disease

D

Patients aged <16y excluding primary CNS		N = 14
Patient sex	Male Female	8 (57%) 6 (43%)
Primary tumour site	Gonadal Retroperitoneal Mediastinal Other/unknown	8 (57%) 0 (0%) 3 (27%) 3 (27%)
Histology	Seminoma Non-seminoma Other/Unknown	1 (8%) 8 (62%) 5 (31%)

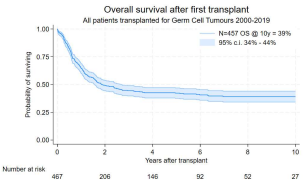
E

Primary CNS		N = 27
Patient sex	Male Female	22 (81%) 5 (19%)
Age at diagnosis (y)	<16 ≥16	16 (59%) 11 (41%)
Histology	Seminoma (germinoma) Non-seminoma Unknown	5 (19%) 4 (15%) 18 (67%)

FIGURES

Figures showing overall survival outcomes in different patient populations. 1: all patients; 2: all patients by year of transplant; 3: adult males aged ≥16y; 4: female patients aged ≥16y by histology; 5: paediatric patients (aged <16y); 6: patients with CNS primary; 7: survival by reported chemotherapy sensitivity ahead of transplant; 8: non-relapse mortality post transplant.

1



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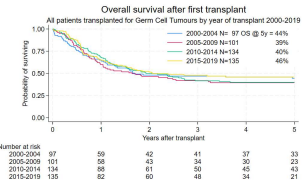

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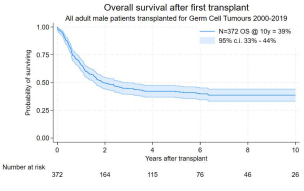

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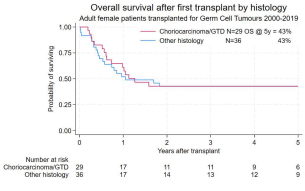

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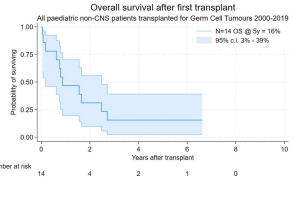

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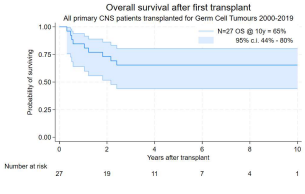

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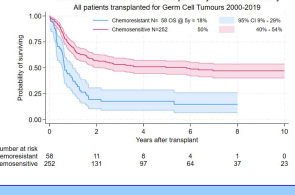

8