Systematic review and meta-analysis on management of relapsed of testicular germ cell tumour after cisplatin-based chemotherapy

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National Germ Cell Group

Introduction

- Approximately 30–40% of patients with poor-risk germ cell tumours (GCTs) relapse despite receiving adequate first-line cisplatin-based chemotherapy
- A subset of these patients develop platinum-refractory disease, associated with a high risk of mortality
- The optimal salvage strategy after cisplatin-based chemotherapy is still under debate
- Comparison between high-dose chemotherapy (HDCT) and conventional-dose chemotherapy (CDCT) is limited by a lack of robust, direct comparative data.

Aims

- To evaluate the efficacy and safety of HDCT versus CDCT in relapsed GCTs by assessing the overall survival (OS), progression-free survival (PFS) and treatment-related mortality

Eligibility

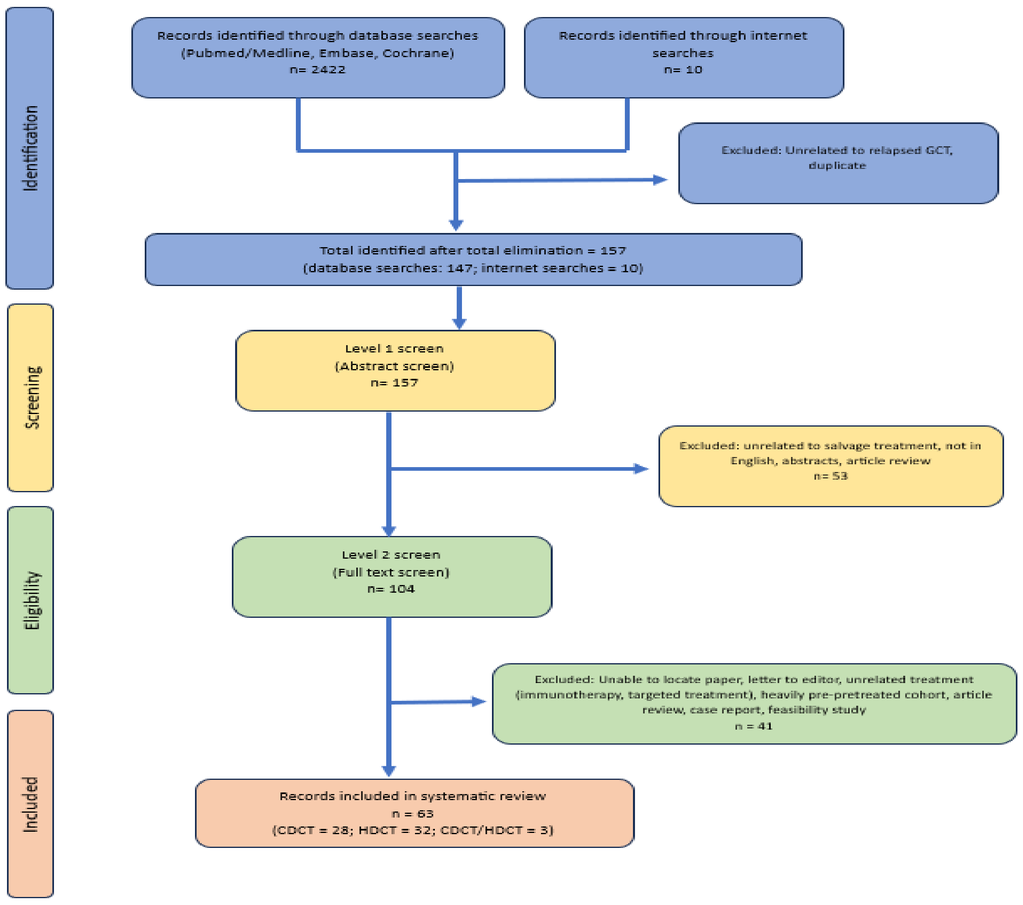
Inclusion Criteria

1. Histologically confirmed advanced germ cell tumours (GCTs), including extragonadal sites (e.g., mediastinum, retroperitoneum).
2. Patients who relapsed after first-line chemotherapy and received second-line or beyond salvage treatment.
3. Patients treated with: Conventional-dose chemotherapy (CDCT), High-dose chemotherapy (HDCT) or Sequential CDCT/HDCT
4. Studies reporting at least one clinical outcome: Progression-Free Survival (PFS), Overall Survival (OS), Objective Response Rate (ORR)
5. Full-text articles available in English

Exclusion Criteria

1. Studies involving: Non-GCT malignancies or non-malignant conditions
2. Studies evaluating non-chemotherapy treatments (e.g., immunotherapy, targeted therapy)
3. Non-original research: case reports, editorials, letters, conference abstracts without full text, or review articles
4. Duplicate publications - only the most updated version of data included

Methodology



- Protocol registered (PROSPERO: CRD42024526637)
- Quality assessed using ROBINS-I
- Meta-analysis in R using meta-package

Results

Category	HDCT	CDCT	Both	
			HDCT	CDCT
Papers included	32	28	3	
Number of patients	2309	1252	1030	1020
Type of study				
Retrospective	17	10	2	
Prospective	15	18	1	
Gender				
Male	1360	1028	956	901
Female	40	4	0	0
NA	909	220	74	119
Median Age	30.8	30.5	29	30
Histology				
Seminoma	443	137	122	106
Non-seminoma / Mixed	1633	896	908	914
Unknown	233	219	0	0
Primary				
Gonadal	1764	934	894	908
Extragonadal	315	177	135	109
Unknown/ not reported	230	141	1	3
Line of treatment				
2nd line	1410	937	1030	1020
3rd line	860	315	0	0
Not reported	39	0	0	0
Platinum				
Sensitive	1332	423	956	901
Resistant	704	146	0	0
Not reported	273	683	74	119
Median follow up (months)	37	36	62	78

Table 1: This table summarises the key characteristics of studies included in a systematic review comparing HDCT and CDCT in relapsed GCTs

Meta analyses

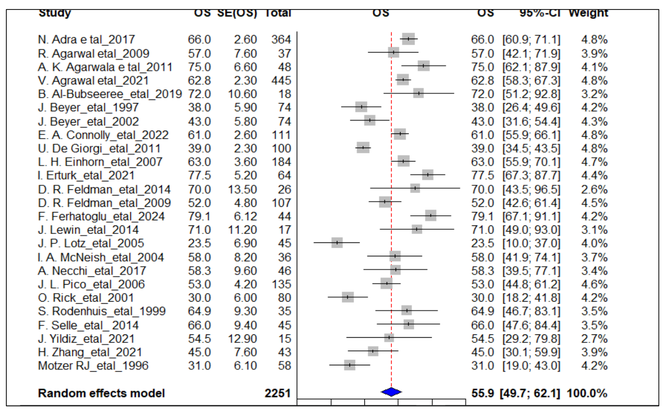


Figure 1: Pooled overall survival following high-dose chemotherapy for relapsed germ cell tumours

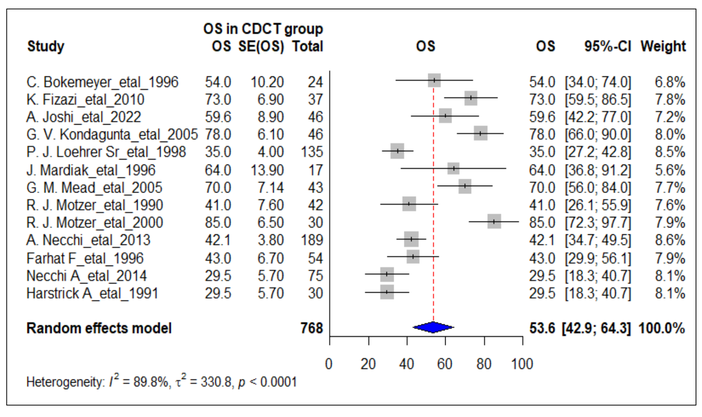


Figure 2: Pooled overall survival following conventional-dose chemotherapy for relapsed germ cell tumours

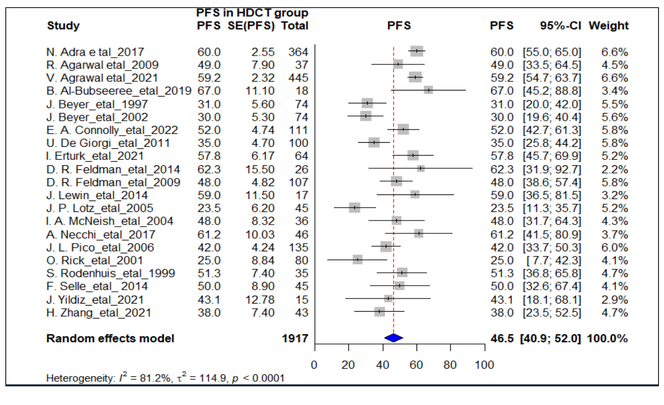


Figure 3: Pooled progression-free survival following high-dose chemotherapy for relapsed germ cell tumours

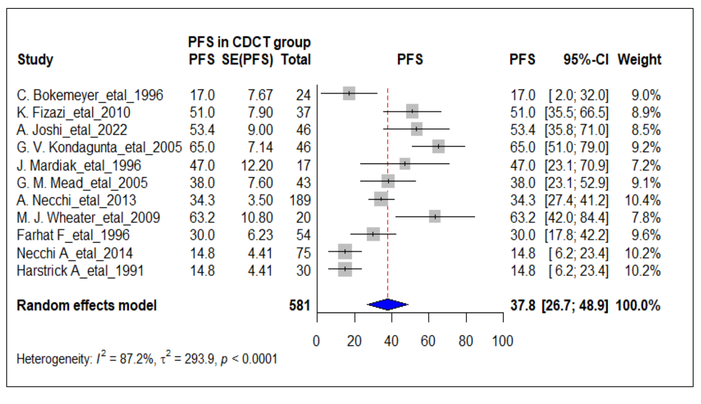


Figure 4: Pooled progression-free survival following conventional-dose chemotherapy for relapsed germ cell tumours

- 63 studies included (n = 5611)
- Overall survival (OS):
  - HDCT: 55.9% (95% CI: 49.7–62.1)
  - CDCT: 53.6% (95% CI: 42.9–64.3)
- Progression-Free survival (PFS)
  - HDCT: : 46.5% (95% CI: 40.9–52.0)
  - CDCT: 37.8% (95% CI: 26.7–48.9)
- Treatment related mortality
  - HDCT: 3.8%
  - CDCT: 1.6%
- No significant publication bias (Egger's p>0.05)
- Interpretation: HDCT showed slightly higher OS and PFS, but overlapping confidence intervals and high heterogeneity (I^2 > 80%) limit definitive conclusions

Conclusion

- The choice between CDCT and HDCT remains uncertain due to variability in trial design, patient selection, treatment regimens and data quality
- The ongoing TIGER trial is expected to provide greater clarity on the optimal salvage approach