Real-world evidence for second-line Paclitaxel, Ifosfamide and Cisplatin chemotherapy to treat recurrent metastatic germ cell tumour

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BACKGOUND

- Most men diagnosed with metastatic germ cell tumour (mGCT) are cured with Bleomycin, Etoposide and Cisplatin (BEP/EP) (ref. 1)
- For those men who develop recurrent mGCT, Paclitaxel, Ifosfamide and Cisplatin (TIP) is an accepted second-line treatment (refs. 2–7)
- We report real-world evidence for TIP as salvage chemotherapy in men diagnosed with recurrent mGCT

METHODS

- Single-centre retrospective cohort study
- Inclusion criteria:
  1. Male patients
  2. Age ≥16 years
  3. First relapse following use of BEP/EP to treat mGCT
- Exclusion criteria:
  1. Consolidation TIP after an unfavorable response to first-line BEP/EP
- Primary efficacy outcome: overall survival (OS)
- Secondary efficacy outcomes: response rates (CR, PR MK-ve, IR, CR(S), treatment failure/early death) and favorable response rate (CR+PR MK-ve)
- Efficacy outcomes were assessed according to:
  1. MSKCC prognostic group: good vs. poor (refs. 2, 8)
  2. Platinum-free interval (PFI): ≥6 vs. <6 months
- Safety outcomes were reported using NCI CTCAE v5.0 criteria
- 3-weekly treatment regimen:
  1. Paclitaxel 175mg/m^2 day 1 (3hr IVI)
  2. Ifosfamide 1200mg/m^2 days 1–5 (2hr IVI)
  3. Cisplatin 20mg/m^2 days 1–5 (4hr IVI)

RESULTS

- Between 01-Jan-2014 and 01-Jan-2023, 24 eligible patients were identified (Table 1)
- Median OS: 39.0 months (95%CI 13.5-not reached; 12 events)
- Follow-up: 6.3–88.6 months (24 patients)
- 4 patients received subsequent HDCT-PBSCT

Age – years	
Median	30
Range	22–62
Original site of GCT – no. (%)	
Gonadal	20 (83)
Extra-gonadal	4 (17) [a]
Histology – no. (%)	
Seminoma	6 (25)
Non-seminoma	9 (38)
Mixed	9 (38)

IGCCCG classification – no. (%)	
Good	16 (37)
Intermediate or poor	8 (33)
TIP cycles – no.	
Median	4
Range	1–6
Total	*111*

Table 1. Patient characteristics. Key: [a] n=3 retroperitoneal and n=1 mediastinal GCT

CTCAE term	Grade 2	Grade 3	Grade 4
Anaemia	22 (92)	17 (71)	0
Neutropenia [a]	14 (58)	10 (42)	12 (50)
Thrombocytopenia	11 (46)	11 (46)	11 (46)
Creatinine increased	5 (21)	1 (4)	0
Nausea	4 (17)	2 (8)	0
Vomiting	4 (17)	1 (4)	0
Fatigue	3 (13)	1 (4)	-
Peripheral neuropathy	3 (13)	0	0
Febrile neutropenia	-	3 (13)	0
Acute kidney injury	-	1 (4)	0

Table 2. Adverse events. Key: Data presented as number of patients (%); [a] All patients received G-CSF; no deaths occurred during chemotherapy.

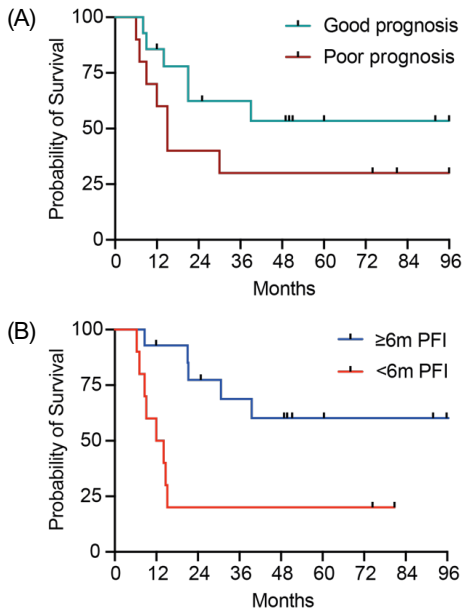

Figure 1. Kaplan Meier estimates for OS
(A) MSKCC prognostic groups
(B) Platinum-free interval

NR vs. 15 months
HR 2.10
95%CI 0.68–6.53
P = 0.16

NR vs. 13 months
HR 4.01
95%CI 1.22–13.68
P = 0.0035

Group (no. of patients)	Response – no. (%)					Favourable response rate % (95%CI) (CR+PR MK-ve)
	CR	PR MK-ve	Complete resection of viable malignancy CR(S)	IR	Treatment Failure/early death	
All patients (24)	3 (13)	18 (75)	1 (4)	0	2 (8)	88% (68–97%)
MSKCC good prognosis (14)	2 (14)	11 (79)	1 (7)	0	0	93% (66–100%)
MSKCC poor prognosis (10)	1 (10)	7 (70)	0	0	2 (20)	80% (44–97%)
PFI ≥6 months (14)	2 (14)	11 (79)	1 (7)	0	0	93% (66–100%)
PFI <6 months (10)	1 (10)	7 (70)	0	0	2 (20)	80% (44–97%)

Table 3: Efficacy outcomes. Key: CR (complete remission): normal AFP and HCG levels and no radiological evidence of residual tumour masses or if surgery was performed, complete excision of mature teratoma or necrotic/fibrotic tissue; PR MK-ve (partial remission, marker negative): normal tumour markers at completion of chemotherapy but nonresectable/resected residual tumour masses; IR (incomplete response): persistently elevated AFP or HCG or viable cancer seen in surgically resected specimens; CR(S): patients with IR and no evidence of disease following complete resection of viable malignancy; Treatment failure: rising tumour markers or radiological progression during chemotherapy.

CONCLUSIONS

- TIP is safe and tolerable
- TIP is associated with an excellent response, although recurrence occurs in >50% of patients
- A platinum-free interval ≥6 months is a better predictor of OS following TIP than MSKCC prognostic groups

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2023 National Germ Cell Group Conference (Glasgow)