Treatment de-escalation for metastatic good-risk seminoma with Carboplatin AUC10: Predictive Factors and Patterns of Relapse

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Introduction

- Carboplatin AUC10 is a de-escalation therapy and serves as an alternative to cisplatin-based chemotherapy (BEP/EP) for patients with good-risk metastatic seminoma
- This de-escalation therapy was introduced to minimise treatment-related toxicity while preserving cure rates
- Some of UK cancer centres have adopted this de-escalation strategy in the management of good-risk metastatic seminoma
- Recent IGCCCG Update 2021 showed improved survival outcomes in cisplatin-based chemotherapy and identified LDH as an adverse prognostic factor within the good-risk group

Objectives

- To provide an updated analysis of survival outcomes using carboplatin AUC10
- To explore patterns of treatment relapse
- To assess the impact of prognostic factors, particularly elevated LDH levels, on survival

Methodology

- Retrospective cohort study conducted from January 2000 to December 2021, with a data cutoff of 31st December 2023
- Data were collected from two centres: St. Bartholomew's Hospital and Mount Vernon Cancer Centre
- Collected variables included age, primary tumour site, disease stage, tumour markers (LDH, AFP, and β-HCG), number of chemotherapy cycles, incidence of relapse, use of salvage treatment, survival status, and cause of death

Results

Baseline characteristics	Number (n= 236)
Median age – years (range)	39 (22–76)
Primary side, n (%)	
Testis	225 (95)
Extragonadal	4 (2)
Retroperitoneum	7 (3)
Stage, n (%)	
IIx	6 (3)
IIa	76 (32)
IIb	79 (33)
IIc	43 (18)
IIIa	6 (3)
IIIb	24 (10)
IIIc	2 (1)
Chemotherapy cycles, n (%)	
3	159 (67)
4	77 (33)
Salvage therapy, n (%)	
BEP	11 (79)
IPO	1 (7)
VIP	1 (7)
Radiotherapy	1 (7)
LDH, n (%)	
<2.5ULN	196 (83)
≥2.5ULN	23 (10)
Unknown	17 (7)

Table 1: Baseline characteristics

Outcome	Age	Months to relapse	Status	Disease related
1. BEP - Radical radiotherapy	58	7	Alive	-
2. BEP - HDCT - Cisplatin/Epirubicin	46	3	Died	Yes
3. IPO	73	6	Died	Yes
4. BEP - HDCT - Cisplatin/Epirubicin	59	13	Died	Yes
5. VIP	65	6	Died	Yes
6. BEP	32	3	Alive	-
7. BEP – HDCT	31	6	Died	Yes
8. Radical radiotherapy to PA nodes	34	88	Alive	-
9. BEP – HDCT – RPLND	39	8	Alive	-
10. BEP – HDCT	39	18	Alive	-
11. BEP	59	6	Died	Unknown
12. BEP – HDCT	37	8	Live	-
13. BEP – Declined HDCT – VeIP	26	6	Died	Yes
14. BEP	53	4	Alive	-

Table 2: Summary of patients who relapsed, detailing first line salvage treatments at relapse and patient outcome

- 14 (6%) patients' relapse
- All relapses occurred within 2 years, except patient 8
- Of the patients who relapsed, 3 (27%) were cured by BEP alone
- The overall salvage rate after carboplatin AUC10 was 50%

Survival analysis

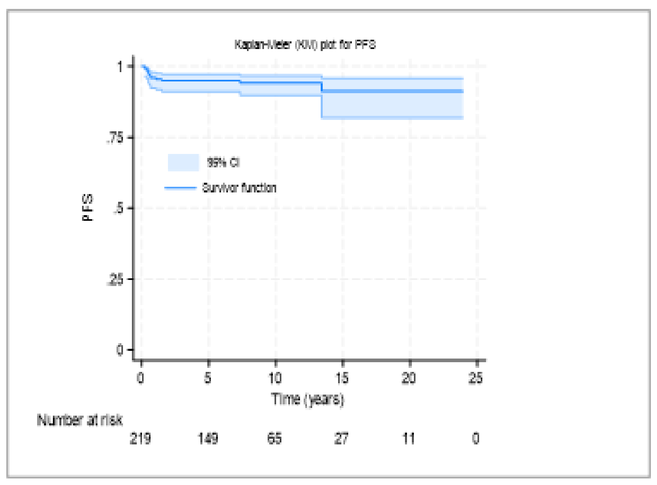

Figure 1: Kaplan-Meier curve showing progression-free survival (PFS)

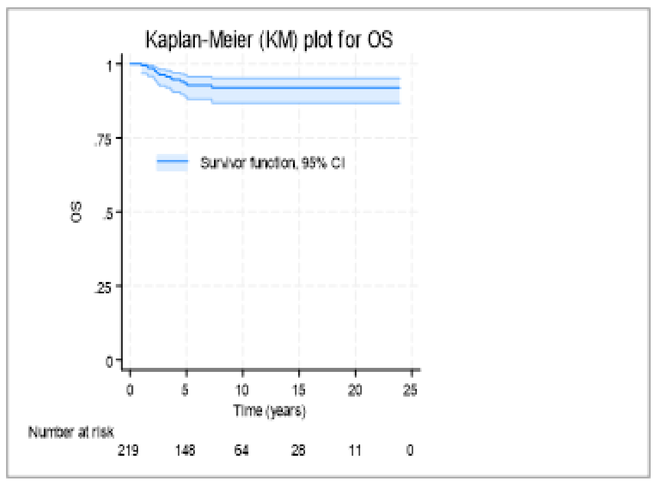

Figure 2: Kaplan-Meier curve showing overall survival (OS)

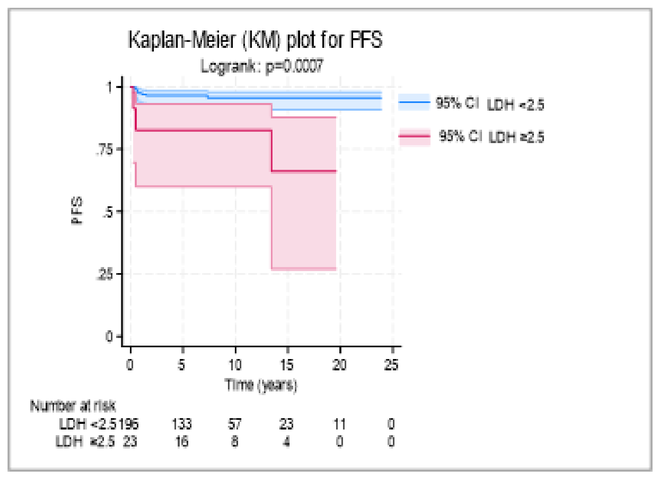

Figure 3: Kaplan-Meier curve showing PFS stratified by LDH levels: <2.5x ULN (blue) and ≥2.5x ULN (red)

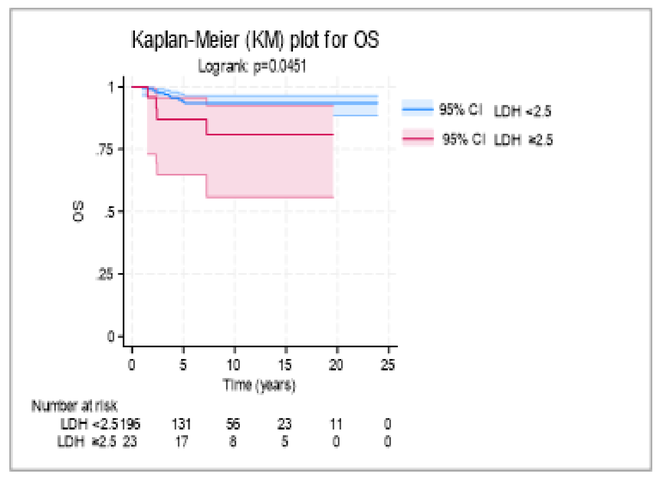

Figure 4: Kaplan-Meier curve showing OS stratified by LDH levels: <2.5 x ULN (blue) and ≥2.5 x ULN (red)

- 5-year PFS was 95% (95% CI: 91% to 97%) (Figure 1) while 5-year OS was 93% (95% CI: 89% to 96%) (Figure 2)
- 5-year PFS for LDH ≥2.5 ULN was 82% (95% CI: 60% to 93%, p=0.0004) (Figure 3) while 5-year OS for LDH ≥2.5 ULN was 86% (95% CI: 65% to 97%, p=0.0369) (Figure 4)

Univariate and multivariate analysis

Variable	Univariate			Multivariate		
	HR	95% CI	p-value	HR	95% CI	p-value
Age at diagnosis						
≤39 years	1					
>39 years	1.06	[0.36, 3.16]	0.914	-	-	-
Stage						
Stage 2	1					
Stage 3	3.7	[1.20, 11.2]	0.023	-	-	-
No cycles						
3 cycles	1					
4 cycles	6.3	[1.72, 23.2]	0.005	4.70	[1.16, 18.8]	0.030
LDH level						
<=2.5 ULN	1					
>2.5 ULN	5.6	[1.82,17.1]	0.003	3.14	[0.71, 14.0]	0.133

Table 3: Results of univariate and multivariate analyses for risk of relapse

Discussion

- **Carboplatin AUC10 outcomes**: 5-year PFS: 95%, 5-year OS: 93% Comparable to IGCCCG Update (PFS 89%, OS 95%)
- **LDH as a Prognostic Factor**: LDH > 2.5ULN associated with poorer outcomes (not statistically significant). 5-year PFS: 82% , 5-year OS: 86% Comparable to IGCCCG Update (3-year PFS 80%, OS 92%)
- **Relapse Patterns**: Majority occur within 2 years. Up to 50% of relapsed patients salvaged, most requiring HDCT
- **Number of Cycles**: No added benefit seen with 4 cycles over 3

Conclusion

- This study represents the largest series of seminoma treated with carboplatin AUC10 and first ever study that look into the impact of LDH on carboplatin AUC10 cohort
- Carboplatin AUC10 offers a promising alternative to cisplatin-based chemotherapy and warrants further investigation through a larger-scale prospective study