UC San Diego Health

Clinical Stage 1 Seminoma Prognosis and ?Adjuvant Therapy

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Friday, March 1, 2024

Key Statistics for Testicular Cancer

The American Cancer Society's estimates for testicular cancer in the United States for 2024 are:

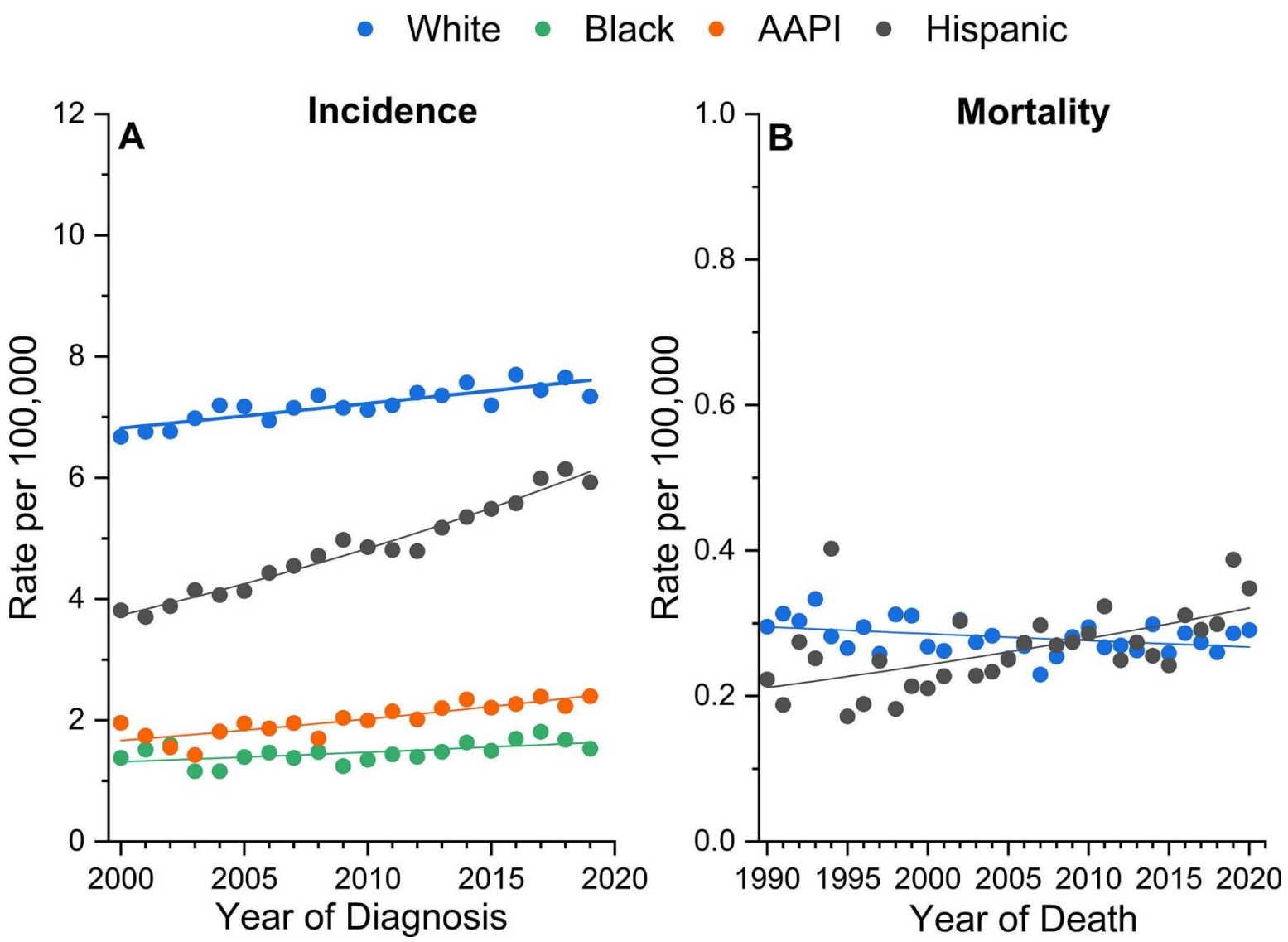
- About 9,760 new cases of testicular cancer diagnosed
- About 500 deaths from testicular cancer

The incidence rate of testicular cancer has been increasing in the US and many other countries for several decades. The increase is mostly in seminomas. Experts have not been able to find reasons for this. Lately, the rate of increase has slowed.

Testicular cancer is not common: about 1 of every 250 males will develop testicular cancer at some point during their lifetime.

The average age of males when first diagnosed with testicular cancer is about 33. This is largely a disease of young and middle-aged men, but about 6% of cases occur in children and teens, and about 8% occur in men older than 55.

Testis Cancer Incidence and Mortality in the 21st Century



SEER Stage Distribution

- Stage 1 localized 70%
- Stage 2 regional nodes 17%
- Stage 3 metastatic 11%
- Unknown/not reported 2%

Therefore:

9760 x 70% = ~6832 cases/year of CS1 testis cancer in the US

Clinical Stage 1 Testis Cancer

~60% seminoma

~40% NSGCT

Clinical Stage 1 Seminoma

Overall CS1 seminoma relapse risk is low.

Do we have any good prognostic schemes to identify high-risk subgroups?

Clinical Stage 1 Seminoma: EAU Prognostic Scheme

Results – Risk Groups

	Relapse Probability and 95% Confidence Interval	
	at 1 Year	at 5 Years
Very Low-Risk: 563 patients (56.4%) TS ≤ 5 cm, no RTI, no LVI TS ≤ 2 cm, either RTI or LVI, but not both	0.04 (0.02 – 0.05)	0.08 (0.06 – 0.11)
Low-Risk: 412 patients (41.3%) TS ≤ 2 cm, both RTI and LVI TS 2 - 5 cm, RTI and/or LVI TS > 5 cm, not both RTI and LVI	0.10 (0.08 – 0.14)	0.20 (0.16 – 0.24)
High-Risk: 23 patients (2.3%) TS > 5 cm, both RTI and LVI	0.30 (0.16 – 0.53)	0.44 (0.27 – 0.66)

Abbreviations: TS = tumor size, RTI = rete testis invasion, LVI = lymphovascular invasion

Clinical Stage 1 Seminoma: EAU Prognostic Scheme

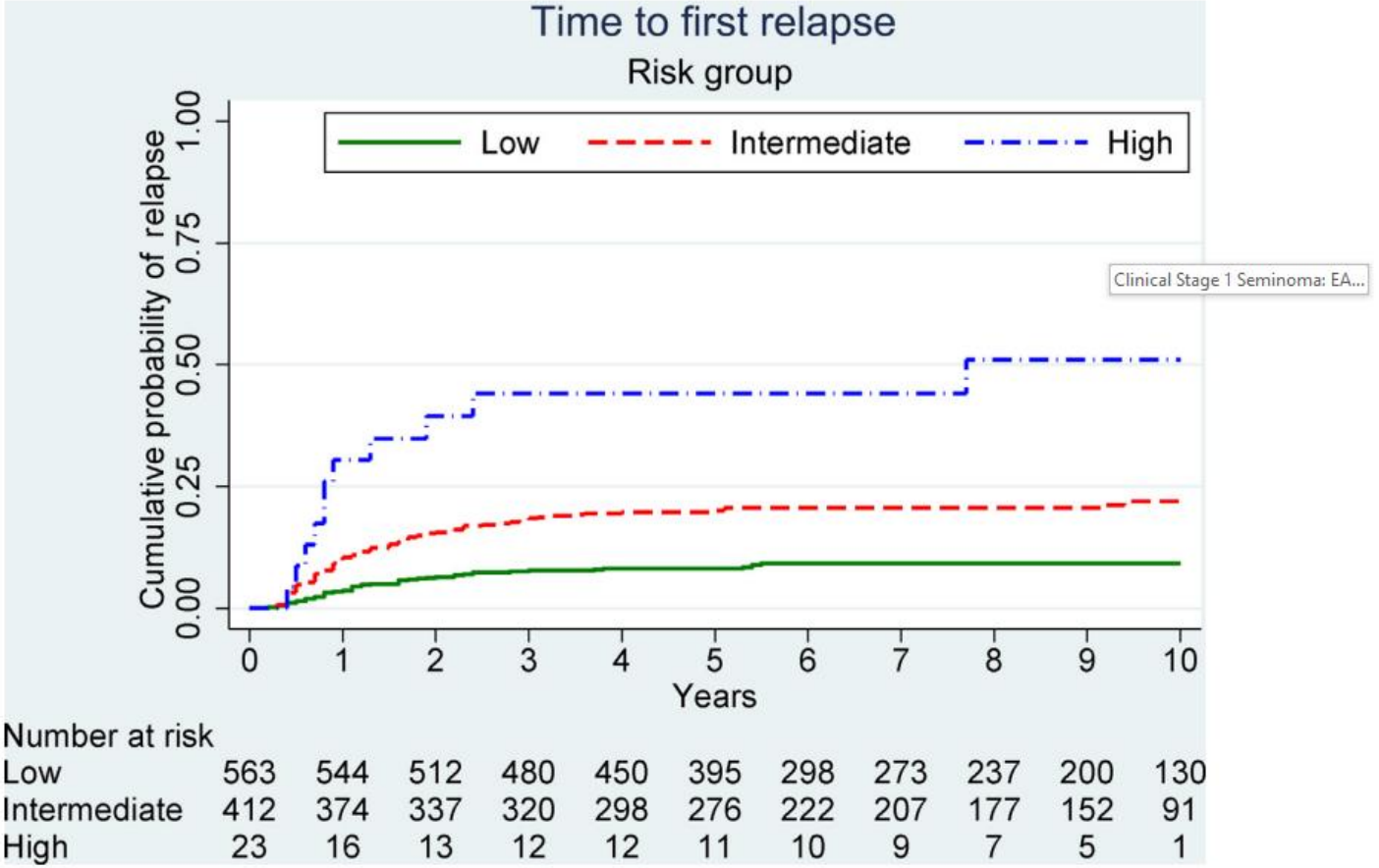


Fig. 1 – Cumulative probabilities of relapse of 998 patients with clinical stage I seminoma germ cell tumor of the testis undergoing active surveillance after radical orchidectomy (discovery cohort), stratified by prognostic factor risk groups based on primary testicular tumor size, rete testis invasion, and lymphovascular invasion.

Clinical Stage 1 Seminoma: Prognostic Scheme from the TRISST trial

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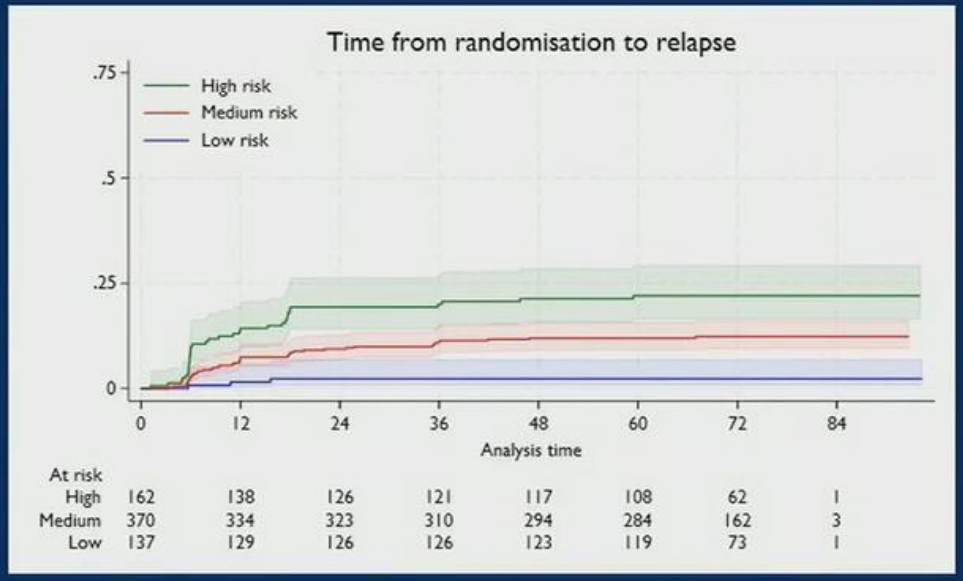
Prognostic model based on TRISST data



- Tumour size ≥4cm and pT3@ were associated with highest risk*
  (≥4cm vs 2cm: HR=4.00, 95% CI 2.00-8.01; pT3 vs pT1: HR=3.89, 1.77-8.57)

Risk group derived in TRISST	% of cohort	5-year relapse risk
Low (age≥30 years, <2cm and pT1)	20%	2.3%
Intermediate (age<30 years and/or 2-4cm and/or pT2@)	55%	12.0%
High (≥4cm and/or pT3)	24%	22.0%

@ pT2 LVI or hilar soft tissue invasion, pT3 spermatic cord invasion
*Rete testis invasion not associated with significant relapse risk

Clinical Stage 1 Seminoma: Prognostic Scheme from the TRISST trial

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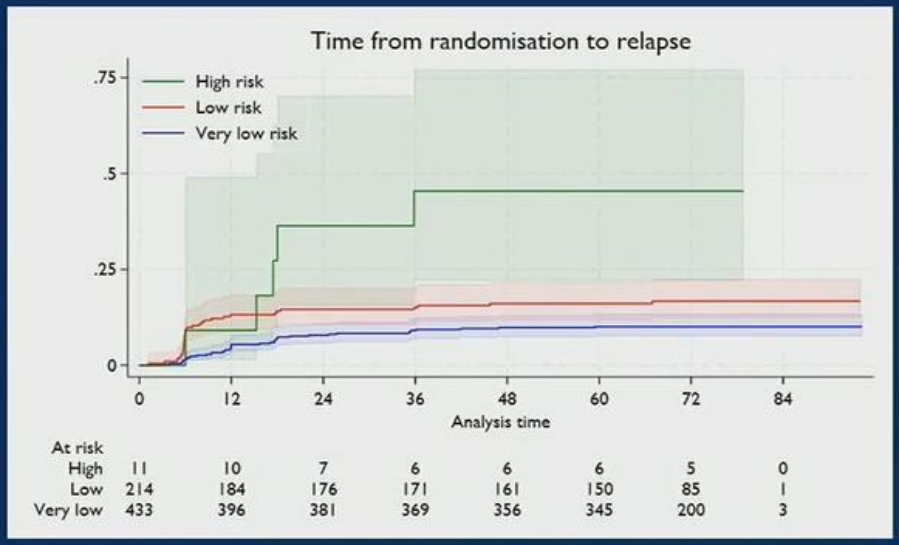
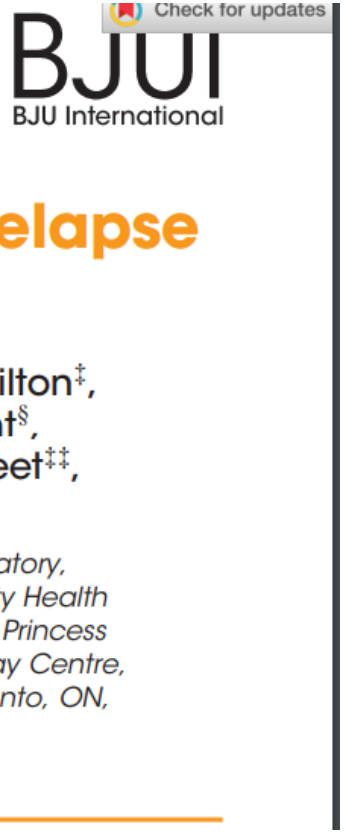
Performance of EAU model for TRISST cohort



- The EAU model was a good fit to TRISST data, Harrell's C-index = 0.62
- Very high risk group only a small proportion of TRISST cohort

EAU risk group applied to TRISST cohort	% of cohort	5-year relapse risk	EAU report
Very low (≤5cm, no RTI and no LVI)	66%	10.1%	8%
Low (≤2cm with RTI and LVI; OR 2-5cm with RTI and/or LVI; OR >5cm with not both RTI and LVI)	33%	16.1%	20%
High (>5cm with both RTI and LVI)	2%	45.5%	44%

Clinical Stage 1 Seminoma: Biomarkers?



Check for updates

BJUI
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Gene expression signatures prognostic for relapse in stage I testicular germ cell tumours

Jeremy Lewin*, Laleh Soltan Ghoraie†, Philippe L. Bedard*, Robert J. Hamilton‡, Peter Chung§, Malcolm Moore¶, Michael A.S. Jewett‡, Lynn Anson-Cartwright§, Carl Virtanen**, Neil Winegarden††, Julie Tsao††, Padraig Warde§, Joan Sweet‡‡, Benjamin Haibe-Kains† and Aaron R. Hansen*

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Small numbers, much work still to be done.

Clinical Stage 1 Seminoma: Biomarkers?

EUROPEAN UROLOGY ONCOLOGY 4 (2021) 483–491

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

European Association of Urology

Editorial by Axel Heidenreich on pp. 492–493 of this issue

Utility of Serum miR-371a-3p in Predicting Relapse on Surveillance in Patients with Clinical Stage I Testicular Germ Cell Cancer

João Lobo[a,b,c,d], Ricardo Leão[e,f,g,h], Ad J.M. Gillis[a], Annette van den Berg[a], Lynn Anson-Cartwright[g,h], Eshetu G. Atenafu[i], Kopika Kuhathaas[g,h], Peter Chung[j], Aaron Hansen[k], Philippe L. Bedard[k], Michael A.S. Jewett[g,h], Padraig Warde[j], Martin O'Malley[l], Joan Sweet[m], Leendert H.J. Looijenga[a,†,], Robert J. Hamilton[g,h,†,*]*

101 seminoma, no useful correlation. Small numbers, much work still to be done—SWOG 1832.

CS1 Seminoma: Adjuvant Therapy

VOLUME 29 · NUMBER 8 · MARCH 10 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Trial of Carboplatin Versus Radiotherapy for Stage I Seminoma: Mature Results on Relapse and Contralateral Testis Cancer Rates in MRC TE19/EORTC 30982 Study (ISRCTN27163214)

R. Timothy D. Oliver, Graham M. Mead, Gordon J.S. Rustin, Johnathan K. Joffe, Nina Aass, Robert Coleman, Rhian Gabe, Philip Pollock, and Sally P. Stenning

See accompanying editorial on page 949

Carboplatin AUC=7 x 1 dose

CS1 Seminoma: Adjuvant Therapy

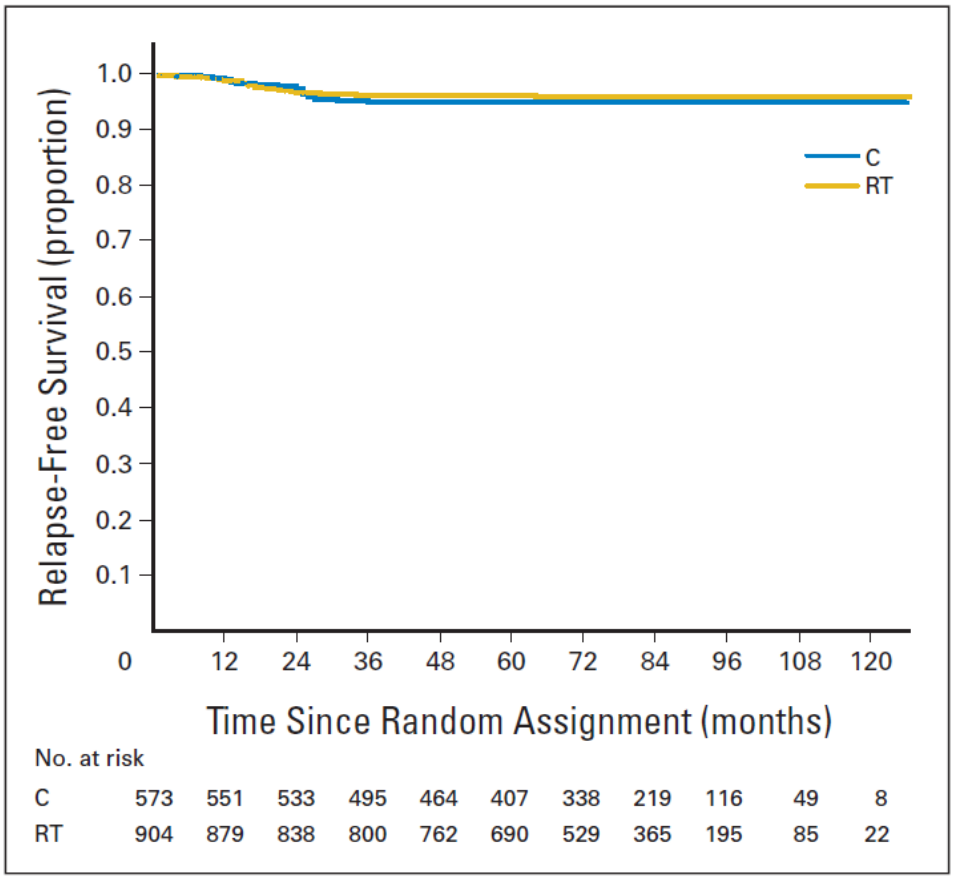

Fig 2. Relapse-free rates (RFRs) by allocated treatment. Intent-to-treat (ITT) analysis (hazard ratio [HR] > 1 favors radiotherapy [RT]): HR, 1.25; 90% CI, 0.83 to 1.89; $P = .37$. Per-protocol analysis (PPA): HR, 1.27; 90% CI, 0.83 to 1.92; $P = .36$. RFR at 5 years: radiotherapy, 96.0% (95% CI, 94.5% to 97.1%); carboplatin (C), 94.7% (95% CI, 92.5% to 96.3%). RFR absolute difference at 5 years: RT-to-C difference, 1.34%; 90% CI, −0.7% to 3.5%.

Relapse rates at 5 years:

Adj carboplatin: 5.3%

Adj XRT: 4.0%

CS1 Seminoma: MRC TE19/EORTC 30982 Trial

Major limitations:

- No surveillance control arm
- Limited patient characteristics presented
- Hard to estimate the magnitude of benefit

CS1 Seminoma: SWENOTECA Database

Annals of Oncology 27: 1299–1304, 2016
doi:10.1093/annonc/mdw164
Published online 6 April 2016

Treatment of stage I seminoma, with one course of adjuvant carboplatin or surveillance, risk-adapted recommendations implementing patient autonomy: a report from the Swedish and Norwegian Testicular Cancer Group (SWENOTECA)

T. Tandstad[1*], O. Ståhl[2], O. Dahl[3,4], H. S. Haugnes[5,6], U. Håkansson[7], Å. Karlsdottir[4], A. Kjellman[8], C. W. Langberg[9], A. Laurell[10], J. Oldenburg[11,12], A. Solberg[1], K. Söderström[13], U. Stierner[14,15], E. Cavallin-Ståhl[2], R. Wahlqvist[16], N. Wall[17,18] & G. Cohn-Cedermark[19,20] on behalf of SWENOTECA

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CS1 Seminoma: SWENOTECA Database

High-risk: size >4cm and/or RTI

- LVI did not hold up in this study

- Patients with 0 or 1 risk factor were recommended to receive 1 dose adj carboplatin
- All others→surveillance
- But actual treatment left to pt and Dr.
- 11.2% had 2 risk factors, but 53% chose adj treatment

CS1 Seminoma: SWENOTECA Database

Three patient groups:

- 469→1 dose adj carboplatin
- 422→surveillance
- Earlier group (221)→1 dose adj carboplatin

CS1 Seminoma: SWENOTECA Database

Recurrence risk at 5.6 years median follow-up

- Overall group: 7.5%
  - No risk factors: 4.0%
  - 1 or 2 risk factors: 15.5%

- Adj carboplatin: 6.2%
  - No risk factors: 2.2%
  - 1 or 2 risk factors: 9.3%
  - 2 risk factors: 10.6%

CS1 Seminoma: adjuvant carboplatin effect on 2nd primary tumors?

MRC TE19 trial reported a reduction in 2nd primaries in the carboplatin group:

- 2 in the carboplatin arm
- 15 in the XRT arm

- However, follow-up 6.5 years may be too short for this endpoint, and at least one other data set did not confirm this.
  - Dieckman K-P et al. J Clin Oncol, 29:2944, 2011

CS1 Seminoma: relapse after adjuvant carboplatin

VOLUME 35 · NUMBER 2 · JANUARY 10, 2017

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Outcome of Men With Relapse After Adjuvant Carboplatin for Clinical Stage I Seminoma

Stefanie Fischer, Torgrim Tandstad, Matthew Wheater, Emilio Porfiri, Aude Fléchon, Jorge Aparicio, Dirk Klingbiel, Breda Skrbinc, Umberto Basso, Jonathan Shamash, Anja Lorch, Klaus-Peter Dieckmann, Gabriella Cohn-Cedermark, Olof Ståhl, Caroline Chau, Edurne Arriola, Kalena Marti, Paul Hutton, Brigitte Laguerre, Pablo Maroto, Jörg Beyer, and Silke Gillessen

185 relapsers
92% treated with chemotherapy
15% had a 2nd relapse
3 patients died from progressive seminoma

CS1 Seminoma: long term complications of adjuvant carboplatin?

Table 1. Overview of studies investigating long-term carboplatin complications in clinical stage I seminoma survivors

Reference	Study period	No. of patients	Study design	Median follow-up	Intervention group	Control group	Long-term effects
Powles *et al.* [15]	1986–2007	199	Prospective database	9.0 years	28 patients two-cycles carboplatin 171 patients one-cycle carboplatin	UK population age and sex matched	No excess overall mortality (SMR 0.89; 95% CI 0.36–1.83), death from circulatory disease (SMR 1.44; CI 0.39–3.69) or incidence of secondary cancers (SIR 0.96; CI 0.26–2.45)
Diminutto *et al.* [10]	2005–2014	115	Retrospective multicenter	22.1 months	115 patients carboplatin		No long-term toxicity reported
Terbuch *et al.* [16]	1994–2013	406	Retrospective cohort study	8.6 years	57 patients RT 37 patients carboplatin	312 patients AS	RT higher CV risk than carboplatin (16 vs. 0%, 95% CI 6 to 25%, $P=0.001$) RT higher CV risk than AS (RD = 11.3%, 95% CI 4.6 to 18%, $P=0.001$)
Chau *et al.* [11]	1996–2013	517	Retrospective analysis	6.5 years	517 patients single-dose carboplatin		17 patients metachronous testicular GCT 6 patients non-GCT tumors
Ghezzi *et al.* [17]	NA	212	Retrospective	24 months	100 patients 1–4 BEP cycles 54 patients one-cycle carboplatin	58 patients AS	12 months BEP group significant reduction in sperm concentration and count ($P<0.0001$) vs. carboplatin and AS groups 24 months significantly higher sperm anomalies ($P<0.05$) than both groups

AS, active surveillance; BEP, bleomycin etoposide cisplatin; CI, confidence interval; CV, cardiovascular; GCT, germ cell tumor; NA, not available; RD, risk difference; RT, radiotherapy; SMR, standardized mortality ratio.

CS1 Seminoma: long term complications of adjuvant carboplatin?

ANTICANCER RESEARCH *35*: 1619-1626 (2015)

Long-term Platinum Retention After Platinum-based Chemotherapy in Testicular Cancer Survivors: A 20-Year Follow-up Study

LINE V. HJELLE[1,2], PER O. M. GUNDERSEN[3], JAN OLDENBURG[4], MARIANNE BRYDØY[5], TORGRIM TANDSTAD[6], TOM WILSGAARD[7], SOPHIE D. FOSSÅ[8,9], ROY M. BREMNES[1,2] and HEGE S. HAUGNES[1,2]

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[3]*Department of Clinical Pharmacology, and* [6]*The Cancer Clinic, St. Olav Hospital, University Hospital, Trondheim, Norway;*
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[5]*Department of Oncology, Haukeland University Hospital, Bergen, Norway;*
[8]*Division of Cancer Medicine and Radiotherapy, Rikshospitalet University Hospital, Oslo, Norway;*
[9]*Medical Faculty, University of Oslo, Oslo, Norway*

Numbers too small for carboplatin alone to draw any conclusions.

CS1 Seminoma: Summary - 1

- Overall relapse risk for CS1 seminoma is low.
- Long term survival is excellent regardless of initial Rx.
- Newer prognostic models may help define a small subset of higher risk patients.
- The magnitude of benefit of adjuvant carboplatin appears to be modest, and exposes many patients to needless drug.
- Long term toxicity of single dose carboplatin remains to be better defined.

CS1 Seminoma: Summary - 2

- Long term imaging F/U is still required after adjuvant carboplatin.

- Surveillance remains the optimal approach for almost all patients.