Treatment Strategies of Testicular Cancer in Norway and Sweden

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Chairman SWENOTECA

SWENOTECA

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informa healthcare

ORIGINAL ARTICLE

The SWENOTECA group: A good example of continuous binational and multidisciplinary collaboration for patients with testicular cancer in Sweden and Norway

Torgrim Tandstad[1], Olof Ståhl[2], Ulf Håkansson[3], Rolf Wahlqvist[4], Olbjørn Klepp[5], Eva Cavallin-Ståhl[2] and Gabriella Cohn-Cedermark[6,7], on behalf of SWENOTECA*

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www.swenoteca.org

SWENOTECA

Display Settings: Abstract

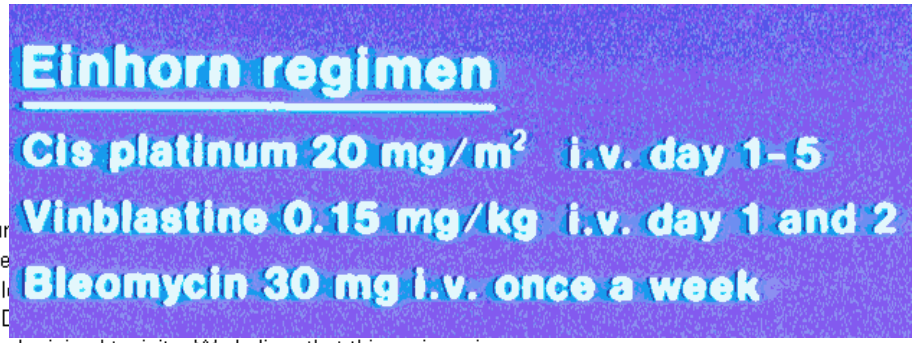
J Urol. 1977 Jan;117(1):65-9.

Improved chemotherapy in disseminated testicular cancer.

Einhorn LH, Donohue JP.

Abstract

Two combination chemotherapy regimens for disseminated testicular cancer are described. Our
bleomycin has been highly successful, producing 16 complete (80 per cent) and 4 partial (20 pe
rendered free of disease by the surgical removal of residual disease, making the effective compl
these patients 16 are alive and 14 are free of disease for more than 8 to more than 20 months. D
weeks of this therapeutic regimen it usually was manageable and maintenance therapy produced minimal toxicity. We believe that this regimen is a
major advance in the management of patients with disseminated testicular cancer.



- The Lugano meeting (in 1980..) inspired the start of the SWENOTECA

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Science and Technology

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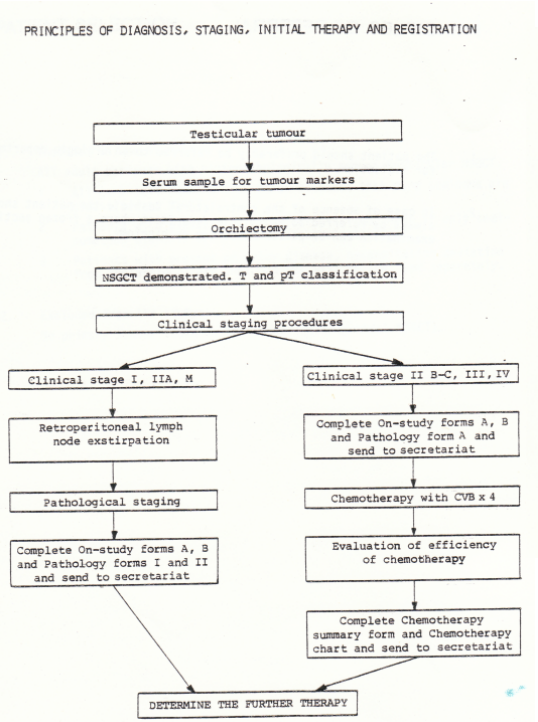
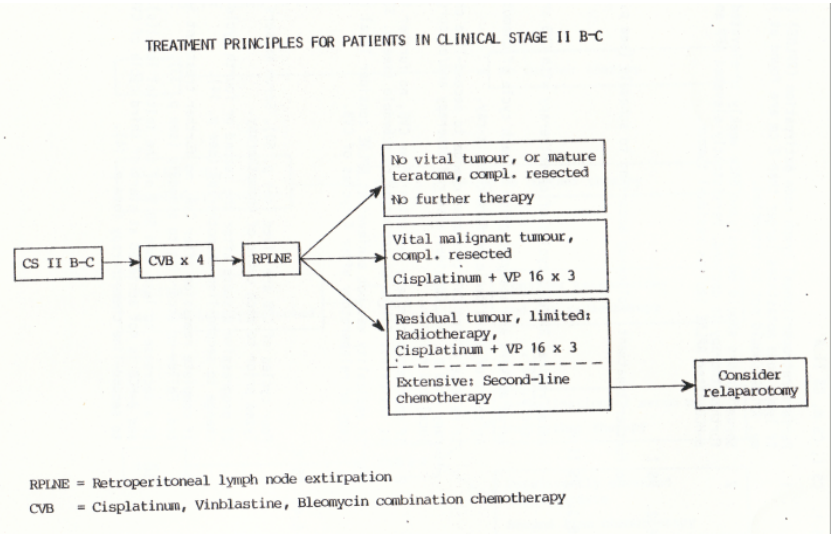
SWEDISH & NORWEGIAN
TESTICULAR CANCER PROJECT
'SWENOTECA'
&
ONCOLOGIC CENTER
LUND, SWEDEN

1.APRIL 1981

TREATMENT OF
NON-SEMINOMATOUS TESTICULAR CANCER





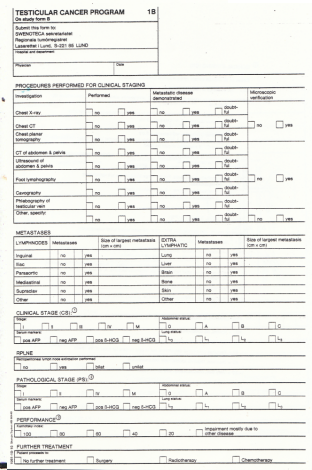
TESTICULAR CANCER PROGRAM **1B**

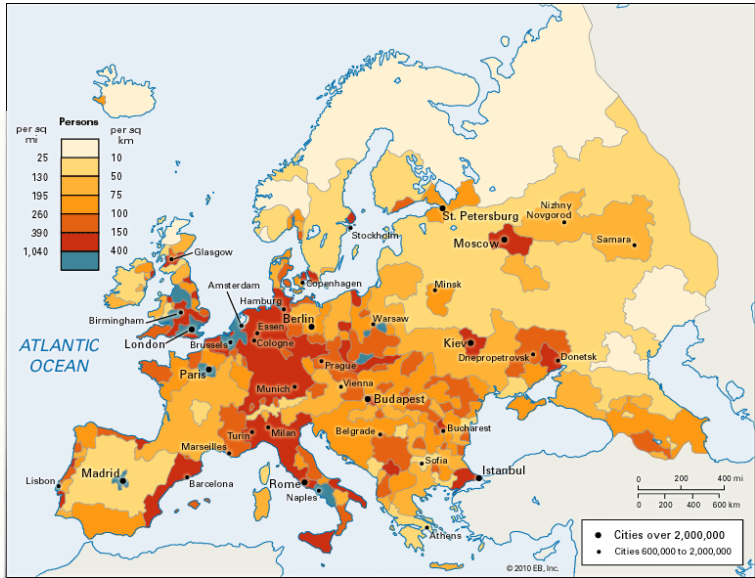
On study form B

Submit this form to:
SWENOTECA sekretariatet
Regionala tumörregistret
Lasarettet i Lund, S-221 85 LUND

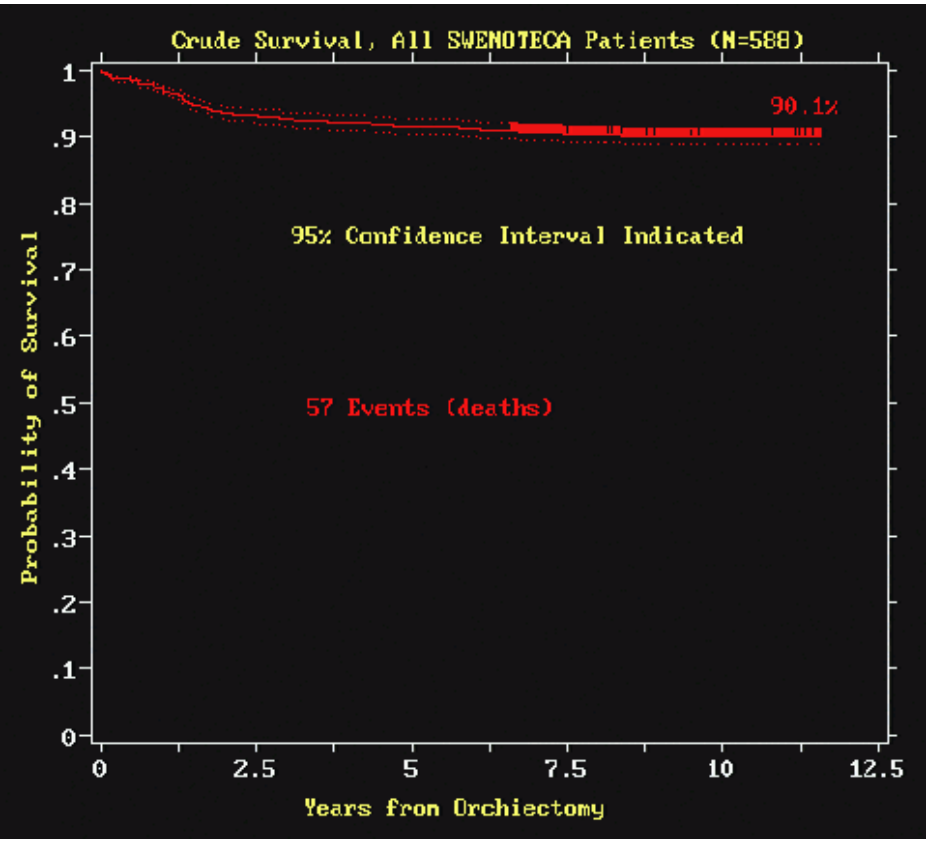
Hospital and department

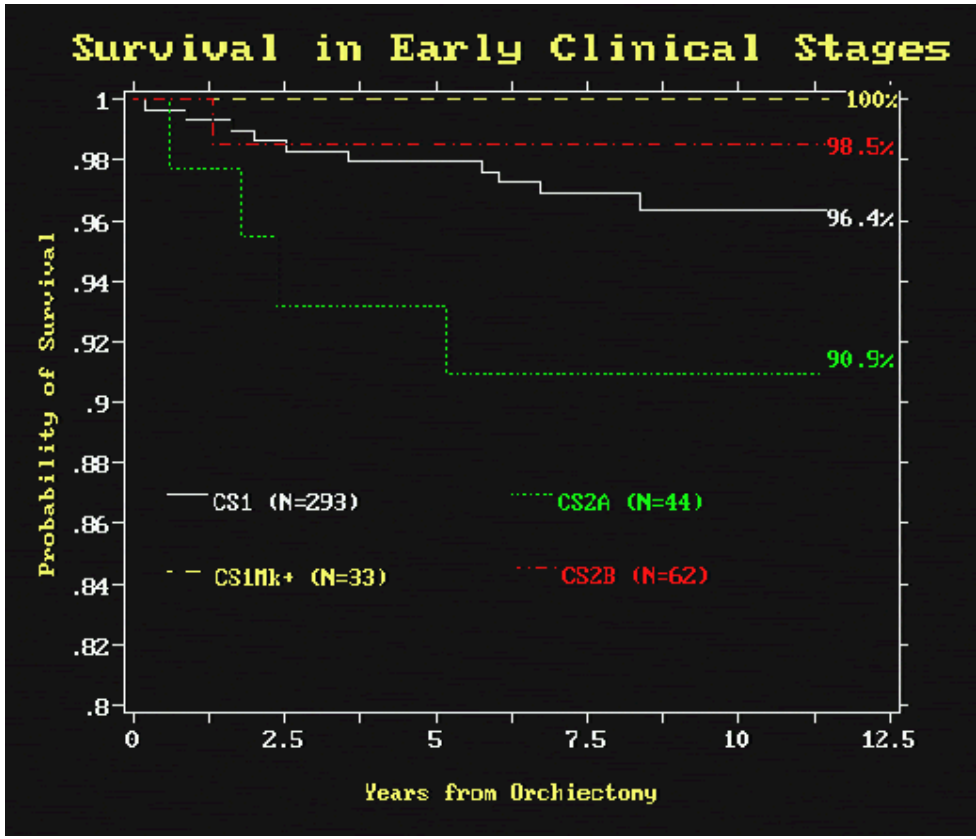
Physician | Date





Standardizing Diagnosis, Treatment and Follow-up





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SWENOTECA

- All patients prospectively registered
- Forms for diagnosis, treatment and follow-up
- National databases

SWENOTECA

- 1981-2000: Nonseminoma only
- 2000-2009: Nonseminoma and seminoma
- 2010-: All germ cell tumours including extragonadal
- Population-based:
  - Currently all hospital treating germ cell tumours in Norway and Sweden
- 600 patients annually

Low Threshold Peer Network

Cazper 30 år Innboks x

Wall Najme <Najme.Wall@regionostergotland.se> 28. mai

til anna.laurell, Arne.Solberg, asa.karlsdottir, Carl, Eva, hege.sagstuen.., jan.oldenburg, Karin, olav.dahl, Olof, meg, ulrika.stierner, ç

svensk › norsk Oversett e-posten Slå av for: svensk

Hej alla kollegor,

Denna man hade initialt en stor embryonal testistumör, markör+ med kärlinväxt, op april 2013 i Västervik. Kom, trots ihärdiga försök telefonledes aldrig till vår mottagning. Har en neuropsykiatrisk sjukdom med sociala fobier.
Dök upp oktober 2014 med massor av metastaser i lungorna, stort konglomerat i buken, njurpåverkan, mkt smärta, skyhöga markörer. Ingen hjärnmetastas. Kom snabbt igång med behandling och fått BEP x 2, BEP-If x 1, PEI x 2 samt 2 högdosbehandlingar med stamcellsstöd. Flertalet sepsisepisoder från början. Klar med behandlingarna och utskriven 8/5.
Markörerna är nu normaliserade och påtagligt regress noteras vid CT 20/5.
Men han fick en kotkompression i L2 december-2014 som nu i retrosepktivet ser snarare ut som skelettmetastas. Retroperitonelala tumören som minskat mkt
flera kotor ser ”fla
tydligare nu när tu

Jag ska skriva till u
förutom att ta ut l
Ska vi istället satsa
Jag beställer MR h

Tacksam för Era sy

Najme. Linköping

Hei,
Dersom han har retroperitoneal tumores > 1 cm ville jeg startet med RPLND. Ostelysene i L1-L3 kan være necrose og en kan vurdere kombinert biopsi og vertebroplastikk i disse virvlene etter RPLND. Vertebroplastikken vil medføre betydelig oppvarming, p.g.a. sement som brukes, og dette kan også bidra til evt. tumorcelledød. Ved viable tumorvevev i benbiopser kan strålebehandling vurderes. Hvor store er lungetumor-restforandringene? Dersom > 1 cm ville jeg adressert de største til slutt dersom markørnene holder seg lave.

Mvh Carl W

Carl
Avdeli
Oslo U
mailto

Hei dere
Jeg er 100% enig med Carl. Strålebehandling nå uten å vite hva som befinner seg i den retroperitoneale residualtumoren eller i columna kan ikke være riktig. Dersom mye teratom (eller lite strålefølsom sekundær somatisk malignitet) vil det vokse etter strålebehandlingen som vil vansl

Arso

hei dere
Støtter Carl og Arnes forslag! Lykke til med videre behandling

Hej mina kollegor,

Cazper opererades den 6/7 med RPLND. En 8 timmar lång operation av ganska svåropererad tumör, konglomerat som satt emot aorta samt njurartär /ven på vänster sida. Det är möjligt att en del av vävnaden sitter fast kvar ovan njurartären som inte gick att operera bort. Postoperativt behandlades på IVA. Drabbas där av övergående SIRS-reaktion med hypertension, takykardi och vätskebehov. I blododling växt av Stafylockus Aureus.
PAD påvisar att i en av 14 uttagna körtlar finns metastas av teratom med 90% nekros. 10% av cellerna är dock viabla. Övriga lgll benigna. Postoperativ kontroll med DT 6/8 visar som tidigare bilaterala lungmetastaser varav några av de största anges minskat ett par mm, men är nu 12 resp. 17 mm. Mjälten är förstorad, Till vä paraaortalt finns nu mjukdelar som minskat från 4.5 x 3 cm till 2.5 x 2 cm. Tillkomst av mjukdelar nedom iliaca communis ca 1 cm. I kotorna L1-L3 sklerotiska förändringar och kompression av L2. Han har något nedsatt njurfunktion med krea som ökat från 90 i april till 125 nu! Nya markörer är på gång men jag har inte aktuella värden. De blev normaliserade under cyt.behandling.

Vad rekommenderar ni som nästa åtgärd?

Med bästa hälsningar/ Najme

SWENOTECA I 1981

- 588 pts with nonseminoma
  - 293 CS I
  - 295 Metastatic

- CS I, CS Mk+, CS IIA: RPLND
  - PS II: CVB x 3

- CS IIB≤: CVB x 4

SWENOTECA I Findings

- CS I: 27% PS II
- LVI: 50% PS II
- CS IIA and normal markers following orchiectomy: 50% PSII
- Dry ejaculation
  - Bilateral RPLND: 56%
  - Unilateral RPLND: 17%
- Survival comparable with best single centre experiences

Prognostic Factors in Clinical Stage I Nonseminomatous Germ Cell Tumors of the Testis: Multivariate Analysis of a Prospective Multicenter Study

By Olbjørn Klepp, Arne M. Olsson, Hans Henrikson, Nina Aass, Olav Dahl, Anna E. Stenwig, Bo-Eric Persson, Eva Cavallin-Ståhl, Sophie D. Fossà, and Lennart Wahlqvist

Journal of Clinical Oncology, Vol 8, No 3 (March), 1990: pp 509-518

Scand J Urol Nephrol 25: 179–190, 1991

EARLY CLINICAL STAGES OF NONSEMINOMATOUS TESTIS CANCER

Evaluation of the Primary Treatment and Follow-up Procedures of the SWENOTECA Project

Olbjørn Klepp,[1] Arne M. Olsson,[2] Sigurd Ous,[3] Stig Nilsson,[4] Per Åge Høisæther[5] and Kjell Tveter[6]

From the Departments of [1]Oncology and Radiotherapy, University Hospital in Trondheim, Norway, [2]Urology, University Hospital in Lund, Sweden, [3]Urology, The Norwegian Radium Hospital, Oslo, Norway, [4]Urology, Sahlgrenska Sjukhuset, Göteborg, Sweden, [5]Urology, University Hospital in Bergen, Norway and [6]Urology, Ullevål Sykehus, Oslo, Norway

Prognostic Factors in Unselected Patients With Nonseminomatous Metastatic Testicular Cancer: A Multicenter Experience

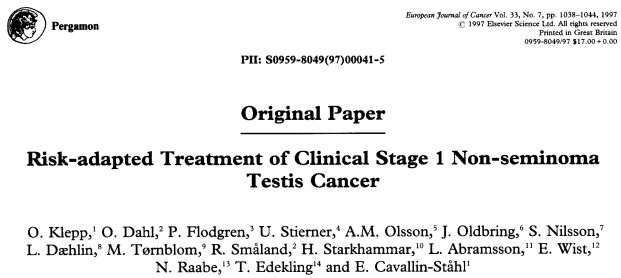
By Nina Aass, Olbjørn Klepp, Eva Cavallin-Ståhl, Olav Dahl, Harriet Wicklund, Bertil Unsgaard, Lars Baldetorp, Sune Ahlström, and Sophie D. Fossà

Journal of Clinical Oncology, Vol 9, No 5 (May), 1991: pp 818-826

CS I Nonseminom

SWENOTECA

SWENOTECA II 1990



Pergamon

European Journal of Cancer Vol. 33, No. 7, pp. 1038–1044, 1997
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PII: S0959-8049(97)00041-5

Original Paper

Risk-adapted Treatment of Clinical Stage 1 Non-seminoma Testis Cancer

O. Klepp,[1] O. Dahl,[2] P. Flodgren,[3] U. Stierner,[4] A.M. Olsson,[5] J. Oldbring,[6] S. Nilsson,[7] L. Dæhlin,[8] M. Tørnblom,[9] R. Småland,[2] H. Starkhammar,[10] L. Abramsson,[11] E. Wist,[12] N. Raabe,[13] T. Edekling[14] and E. Cavallin-Ståhl[1]

- CS I Nonseminoma, first attempt of risk adapted treatment using results from SWENOTECA I
  - CS I: 250 patients, risk groups based on LVI and level of AFP before orchiectomy
    - Low risk: Surveillance
    - Intermediate risk: RPLND, PS II: BEP x 3
    - High risk: BEP x 3
  - Results
    - First study ever with 100% overall survival in CS I nonseminoma
    - Confirmed LVI as a risk factor for relapse
    - Concluded with no place of adjuvant RPLND as adjuvant treatment

SWENOTECA III 1995

original article

Annals of Oncology
doi:10.1093/annonc/mdq026

Long-term follow-up after risk-adapted treatment in clinical stage 1 (CS1) nonseminomatous germ-cell testicular cancer (NSGCT) implementing adjuvant CVB chemotherapy. A SWENOTECA study

T. Tandstad[1]*, G. Cohn-Cedermark[2], O. Dahl[3], U. Stierner[4], E. Cavallin-Stahl[5], R. M. Bremnes[6] & O. Klepp[7]

- CS I Nonseminoma, redefined risk adapted treatment using results from SWENOTECA II, 232 pts
  - Risk groups based on LVI
    - Low risk, LVI-: Surveillance or CVB x 1Low risk: Surveillance
    - High risk, LVI+: CVB x 2
  - Results
    - Surveillance and LVI-: 13% relapse
    - CVB: High rate of gastrointestinal toxicity, CVB x 1 inadequate effect
    - Concluded with no place of adjuvant CVB

VOLUME 27 · NUMBER 13 · MAY 1 2009
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

SWENOTECA III/VI 1997

- LVI+: BEP x 2, reduced to BEP x 1
- LVI-: BEP x 1 or surveillance

Risk-Adapted Treatment in Clinical Stage I Nonseminomatous Germ Cell Testicular Cancer: The SWENOTECA Management Program

Torgrim Tandstad, Olav Dahl, Gabriella Cohn-Cedermark, Eva Cavallin-Stahl, Ulrika Stierner, Arne Solberg, Carl Langberg, Roy M. Bremnes, Anna Laurell, Hans Wijkstrøm, and Olbjørn Klepp

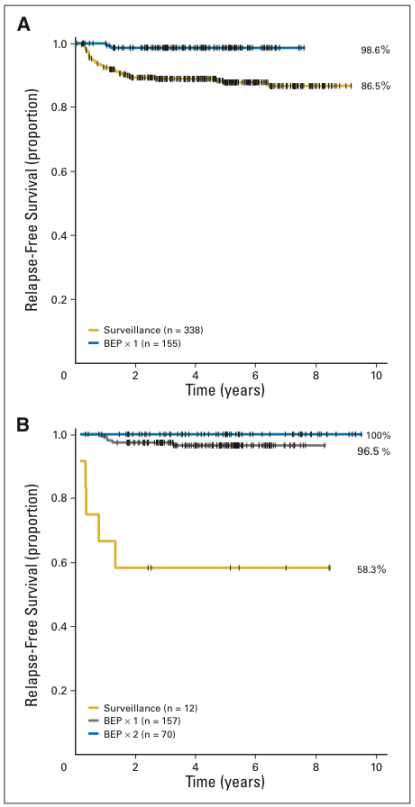

Table 3. Relapse Rates, Time to Relapse, and Duration of Follow-Up

Risk Group	ACT	No. of Patients	Relapse		Kaplan-Meier Relapse Rate (%)	Time to Relapse (years)		Median Observation Time (years)
			No.	%		Median	Range	
All patients		745	51	6.8	7.9	0.8	0.2-6.4	4.7
VASC+	None	12	5	41.7	41.7	0.4	0.2-1.3	5.3
VASC+	BEP × 1	157	5	3.2	3.5	1.1	0.9-3.3	4.8
VASC+	BEP × 2	70	0		0			5.0
VASC−	None	338	39	11.5	13.2	0.7	0.2-6.4	5.0
VASC−	BEP × 1	155	2	1.3	1.4	1.2	1.0-1.2	4.1
VASC−	BEP × 2	2	0		0			2.9
Other		11	0		0			4.8

Abbreviations: ACT, adjuvant chemotherapy; VASC+, with vascular invasion; VASC−, without vascular invasion; BEP, bleomycin, etoposide, and cisplatin.

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Annals of Oncology

original articles

Annals of Oncology 25: 2167–2172, 2014
doi:10.1093/annonc/mdu375
Published online 11 August 2014

SWENOTECA III/VI 1997

- Mature and expanded data on BEP x 1 published in 2014
- Median follow-up 7.9 years
- 517 patients

One course of adjuvant BEP in clinical stage I nonseminoma mature and expanded results from the SWENOTECA group

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

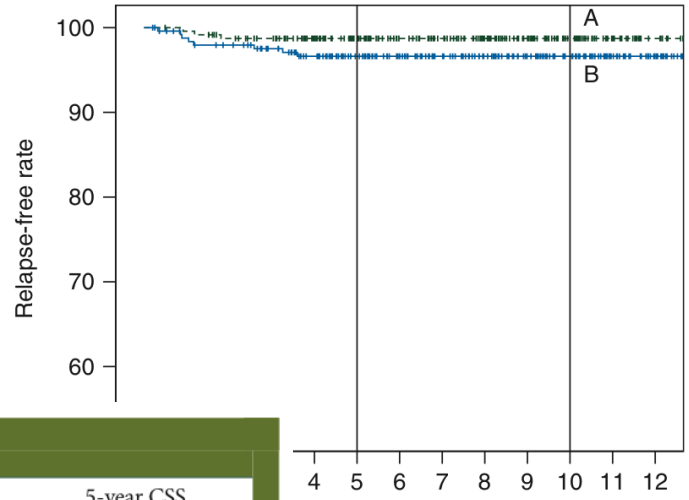

Table 2. Duration of follow-up, relapse rates, time to relapse, and survival

Risk group	No. of patients	Median age (range), years	Median follow-up (years)	Relapses		Time to relapse (years)		5-year OS, 10-year OS (%)	5-year CSS, 10-year CSS (%)
				No.	K-M RR (%)	Median	Range		
All	517	29 (15–71)	7.9	12	2.4	12	0.3–3.6	99.0, 96.9	100, 99.6
With LVI	258	29	8.0	8	3.2	1.1	0.3–3.6	98.7, 96.9	100, 99.3
Without LVI	255	30	7.9	4	1.6	1.2	0.9–1.8	99.2, 96.9	100, 100
LVI uncertain	4	30	6.1	0	0			100, 100	100, 100

K-M RR, relapse rate, estimated using Kaplan–Meier survival curves; OS, overall survival estimated using Kaplan–Meier survival curves; CSS, cause-specific survival estimated using Kaplan–Meier survival curves; LVI, lymphovascular invasion.

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SWENOTECA III/VI 1997

Table 4. Assumed burden of chemotherapy, different treatment strategies

Treatment	All[a]		LVI+		LVI–	
	Surveillance[b]	BEP × 1[c]	Surveillance[b]	BEP × 1[c]	Surveillance[b]	BEP × 1[c]
Number of patients	1000	1000	1000	1000	1000	1000
Relapses	250	21	500	32	150	16
Total number of chemotherapy courses given	735	1030	1470	1072	441	1012
Patients exposed to salvage therapy i.e. ≥3 courses of chemotherapy	245 (24.5%)	10 (1%)	490 (49%)	23 (2.3%)	147 (14.7%)	4 (0.4%)

[a]Assuming: one-third of patients with lymphovascular invasion (LVI) and two-third of patients without LVI.
[b]Based on a risk of relapse of 50% in patients with LVI, 15% in patients without LVI and 25% in an unselected population.
[c]Based on treatment results from this study, where only 25% of relapsing patients without LVI and 75% of patients with LVI required salvage chemotherapy.

- As few patients as possible should be exposed to salvage treatment
- As few patients as possible should be exposed to unnecessary adjuvant treatment

SWENOTECA VIII (2012-current)

- Delayed second staging 6-8 weeks after orchiectomy
- LVI-
  - Surveillance, but can choose BEP x 1
- LVI+
  - BEP x 1 recommended

Metastatic nonseminoma

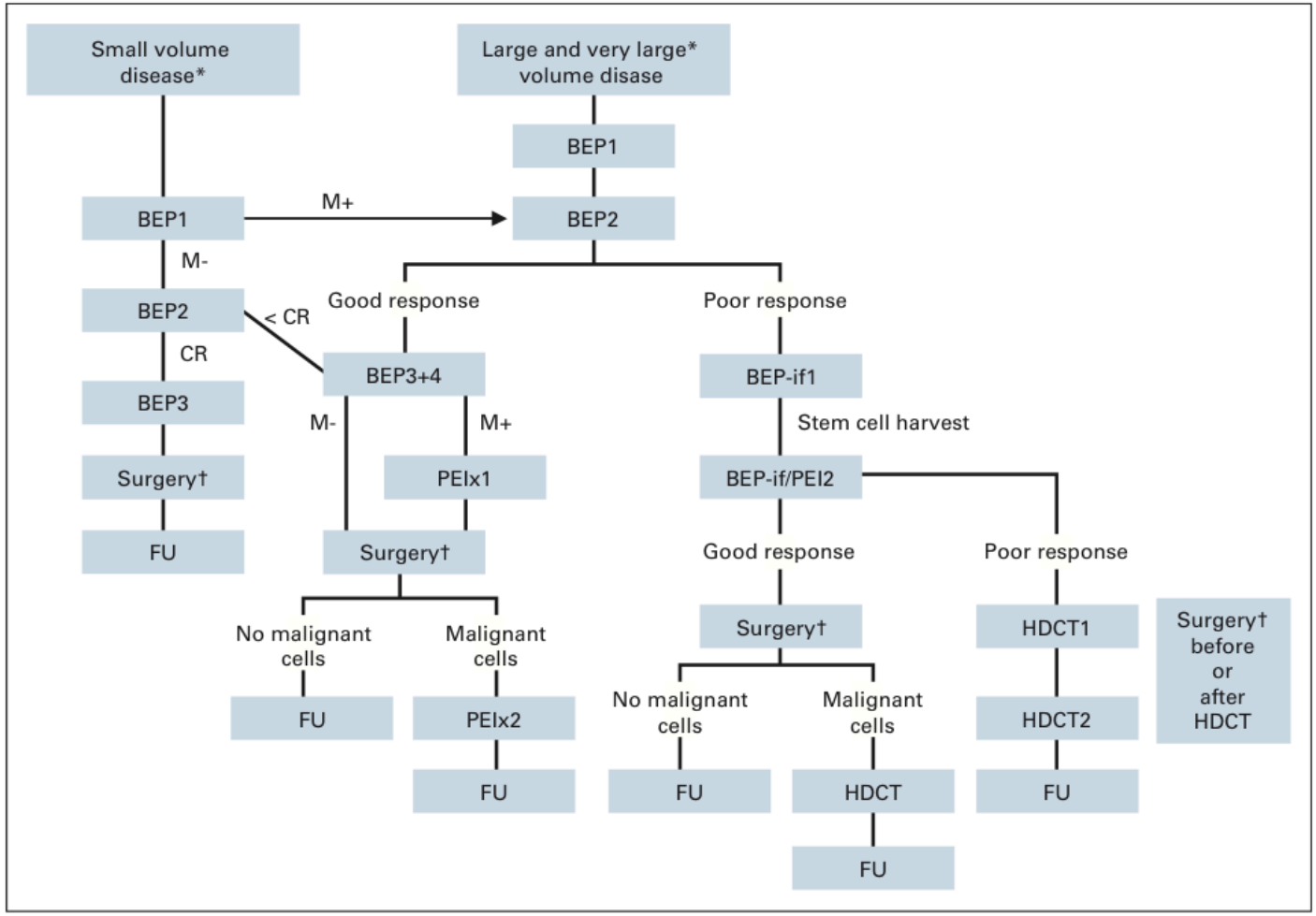
SWENOTECA

SWENOTECA IV 1995

- Metastatic nonseminoma
  - Before the IGCCCG-classification
  - Data on the prognostic value of tumor marker decline was available

- Markers measured day 1, 5 and 15 every cycle
  - Decline evaluated from highest level (usually day 5)

SWENOTECA IV



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SWENOTECA IV

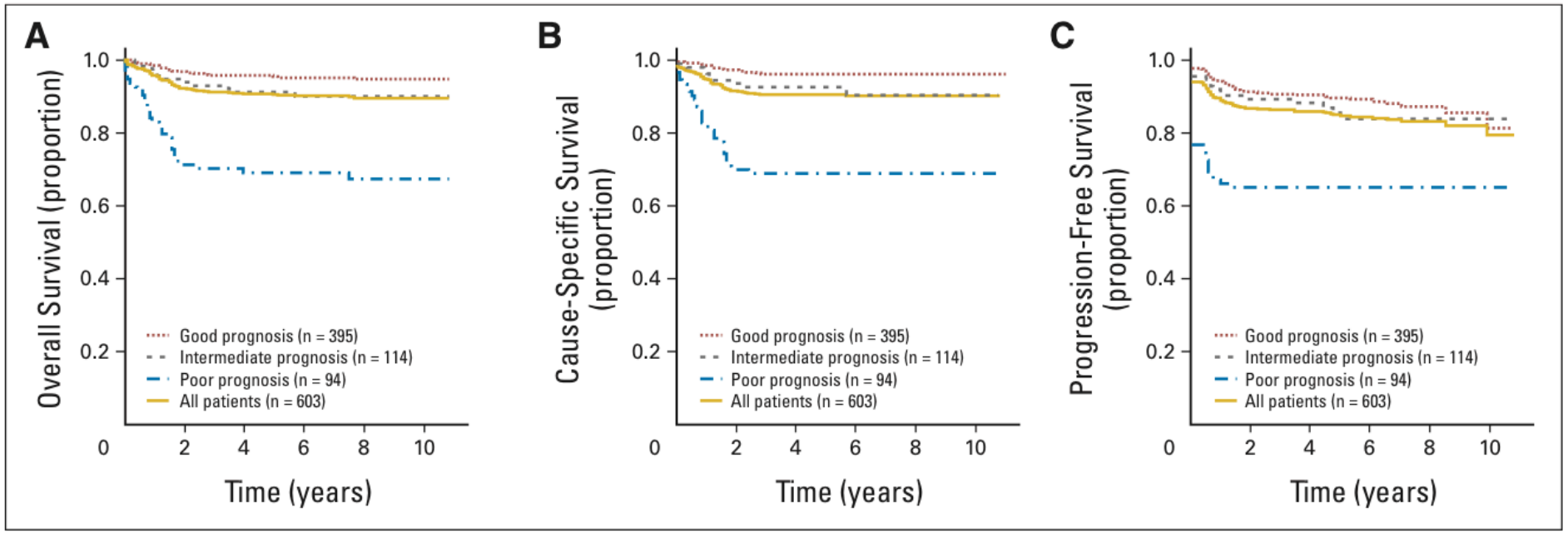


Fig 2. Survival of all 603 patients with metastatic nonseminomatous germ cell tumors according to the International Germ Cell Consensus Classification. (A) Overall survival; (B) cause-specific survival; (C) progression-free survival.

SWENOTECA IV

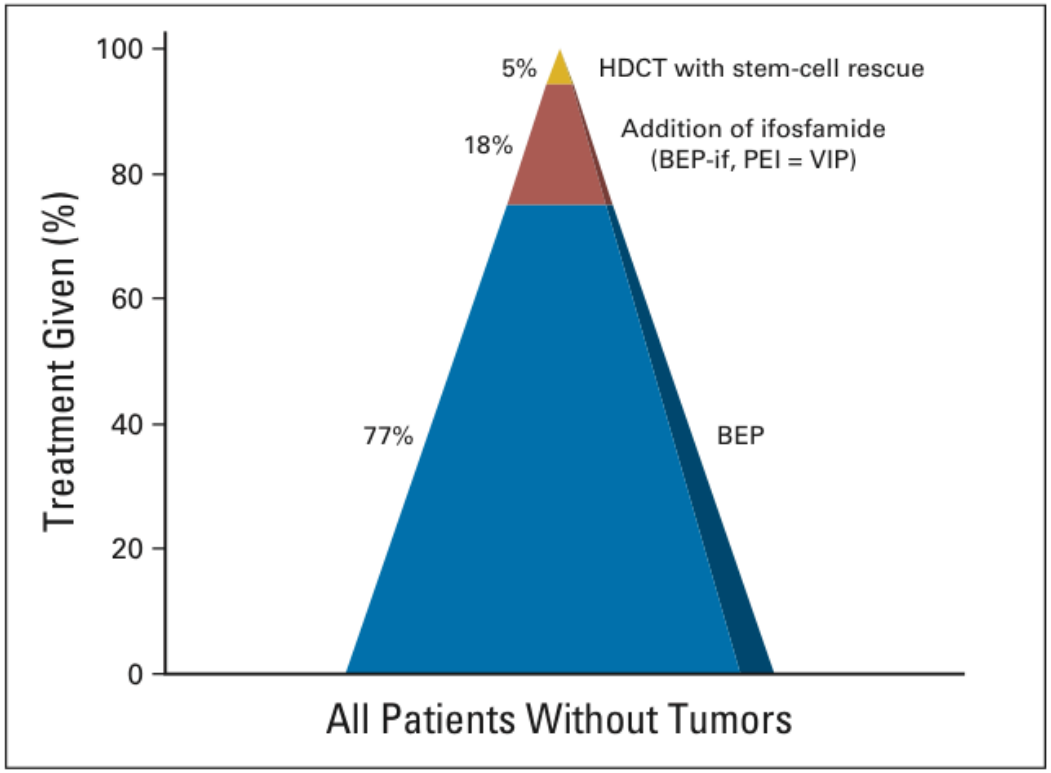
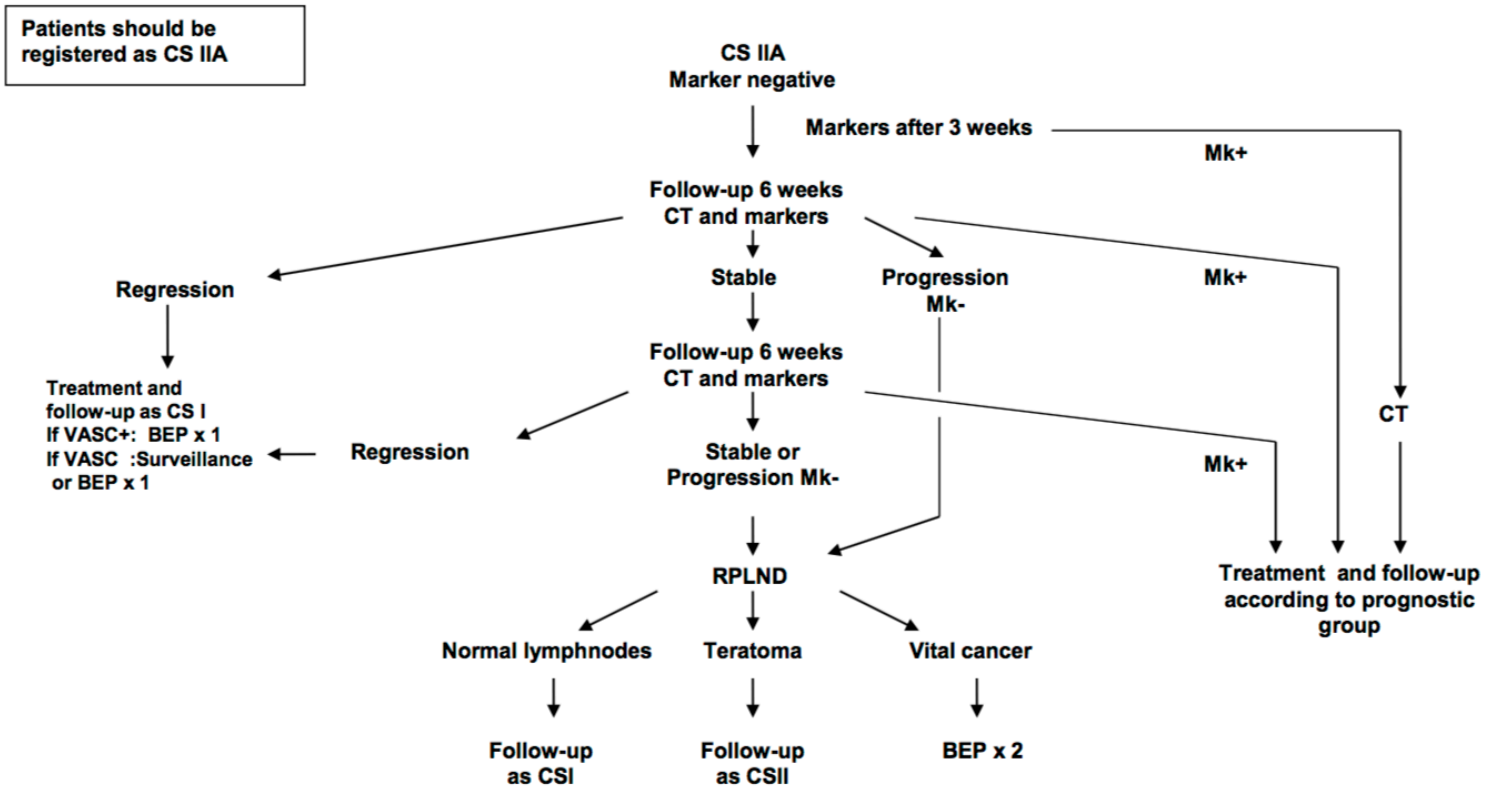


Fig 3. Proportions according to treatment intensity in patients who were tumor free after the primary treatment. HDCT, high-dose chemotherapy; BEP-if, BEP plus ifosfamide and mesna; BEP, bleomycin, etoposide, and cisplatin; PEI = VIP, etoposide and cisplatin plus ifosfamide and mesna.

SWENOTECA VIII (2012-current)

Clinical stage IIA marker negative at definitive staging



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SWENOTECA VIII (2012-current)

Non-seminoma clinical stages Mk+, IIA Mk+, III, IV

Marker t ½ on time:
AFP ≤7 days
ßHCG ≤3 days
Marker t ½ delayed:
AFP >7 days
ßHCG >3 days

Good prognosis

BEP x 2

Response evaluation* — **t½ on time** — **t½ delayed → go to intermediate**

BEP x 1

Response evaluation — **t½ on time** — **t½ delayed → go to intermediate**

±RPLND and other tumour resection

No vital cancer | **Vital cancer**

FU ← **PEI x 2**

***Primarily Mk- at final staging:**
If radiological regression after 2 cycles is < 25%, surgery is recommended

Marker progress:
see protocol for alternative strategies
Reevaluate-
Sanctuary met? (brain, bone)
Other testis?
Consider surgery

RPLND if not CR (<1 cm)

Other residual tumours should be resected if possible.

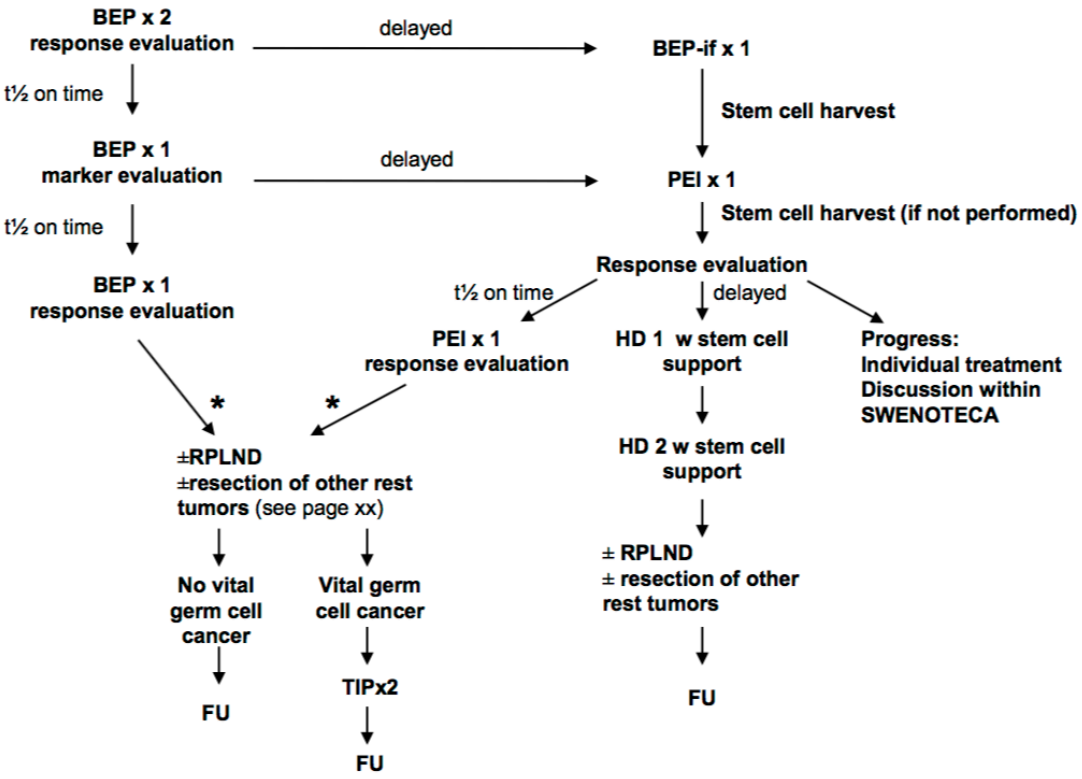
SWENOTECA VIII (2012-current)

"Poor markers":
AFP >10 000ng/ml
ßHCG >50 000 IU/L
LD >10x upper limit of normal

Marker t ½ on time:
AFP ≤7 days
ßHCG ≤3 days

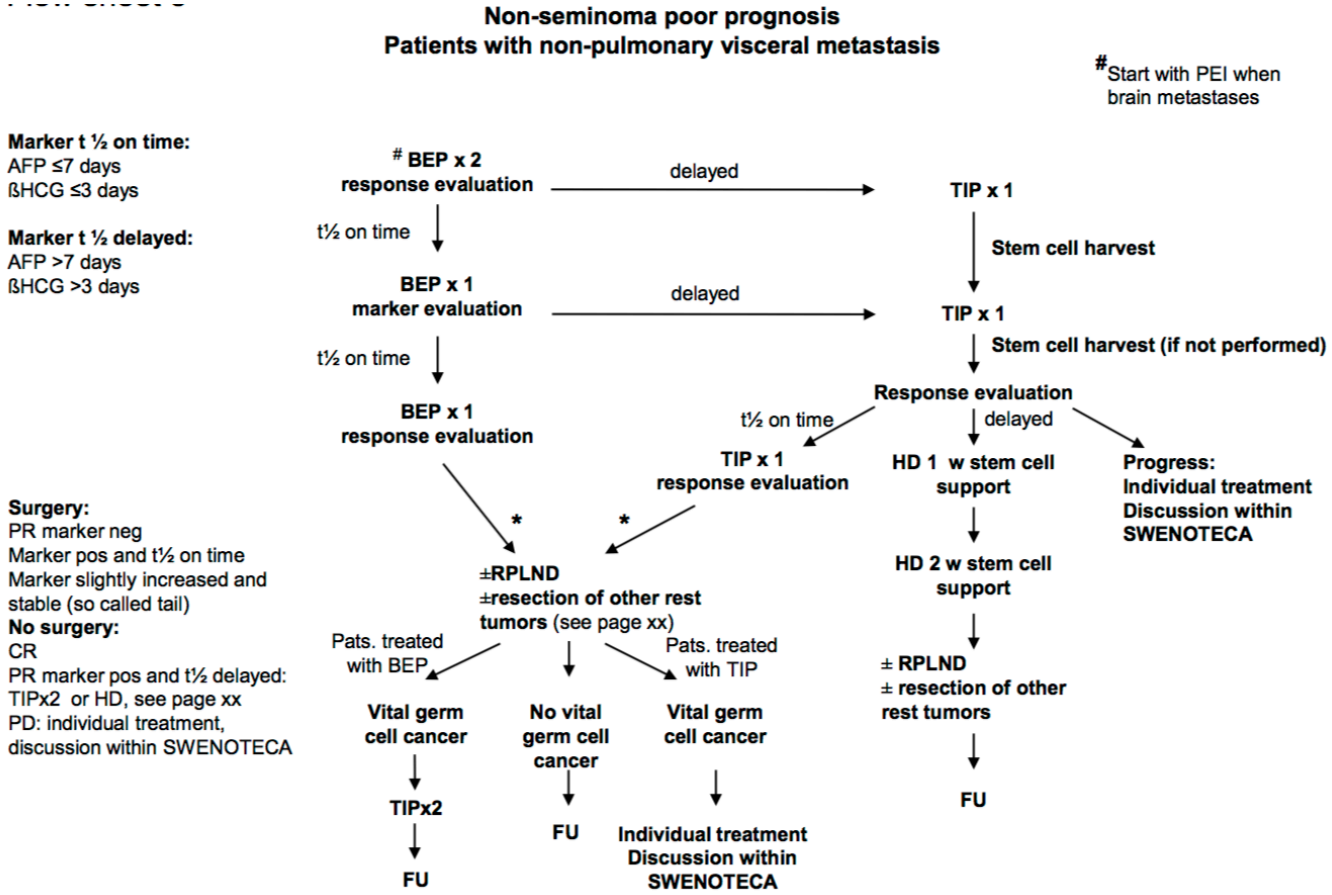
Marker t ½ delayed:
AFP >7 days
ßHCG >3 days

Patients with intermediate prognosis and patients with poor prognosis due to "poor markers" only and no non-pulmonary visceral metastasis



* **Surgery:**
PR marker neg
Marker pos and t½ on time
Marker slightly increased and stable (so called tail)
No surgery:
CR
PR marker pos and t½ delayed: TIPx2 or HD, see page xx
PD: individual treatment, discussion within SWENOTECA

SWENOTECA VIII (2012-current)



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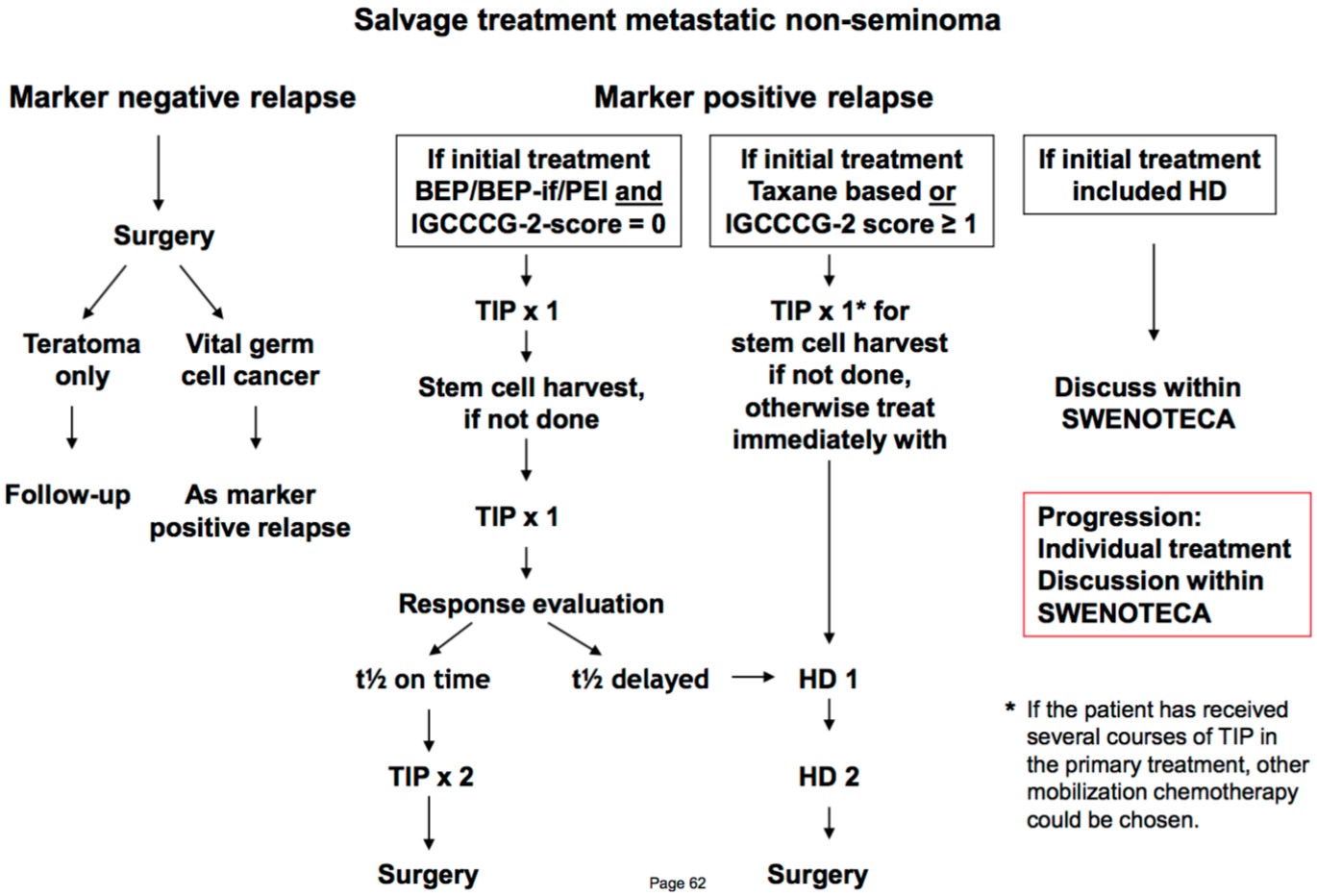
SWENOTECA VIII (2012-current)



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Seminoma

SWENOTECA

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

SWENOTECA V 2000

Management of Seminomatous Testicular Cancer: A Binational Prospective Population-Based Study From the Swedish Norwegian Testicular Cancer Study Group (SWENOTECA)

Torgrim Tandstad, Rune Smaaland, Arne Solberg, Roy M. Bremnes, Carl W. Langberg, Anna Laurell, Ulrika K. Stierner, Olof Ståhl, Eva K. Cavallin-Ståhl, Olbjørn H. Klepp, Olav Dahl, and Gabriella Cohn-Cedermark

- First protocol for seminoma
- 1384 patients
- CS I
  - Radiotherapy
  - Surveillance
  - (Carboplatin)
- CS IIA
  - Radiotherapy
- CS IIB≤
  - EP x 4

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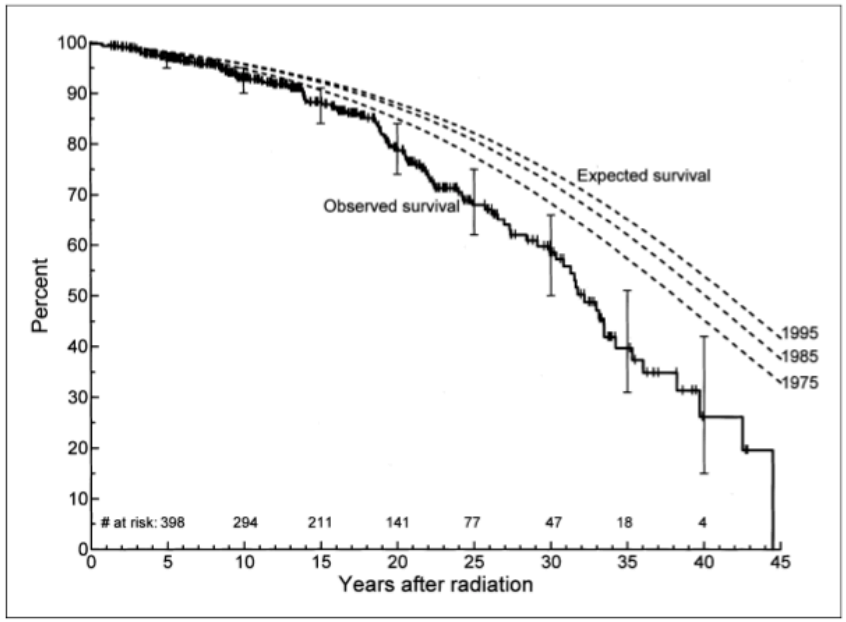

Fig 1. Survival of all 453 patients. Vertical bars are 95% CIs. The number of men at risk is shown above the abscissa. The individually age- and race-adjusted expected survival curves from life-tables for the male US population in 1975, 1985, and 1995 are also shown. These survival curves give the age- and race-adjusted expected survival rates for individuals subjected to the force of mortality in the US male population for that year.

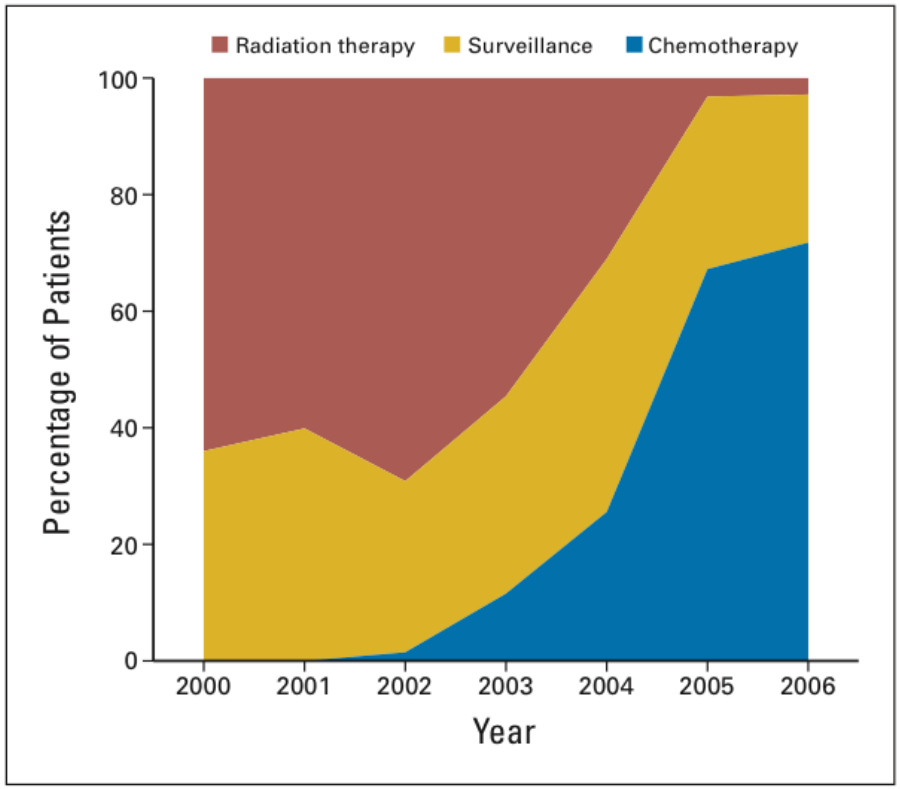

Fig 1. Development in the treatment of clinical stage 1 seminoma, 2000 to 2006.

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Table 1. Stage, Treatment, Follow-Up, Relapse, and Survival

CS					Median			Median						
RMH	AJCC	%	Treatment	No. of Patients	Age (years)	IQR	Range	Follow-Up (years)	IQR	Range	RFI (%)	No. of Relapses	5-Year OS (%)	5-Year CSS (%)
All patients		100		1,384 (total)	37	31-45	16-86	5.2	3.8-6.6	0.1-10.2	92.6	90	98.1	99.6
1	1	86.1	All CS1		37	31-44	16-86	5.1	3.7-6-6	0.1-10.2			98.5	99.9
			Radiotherapy*	481	37	31-45	17-84	6.1	5.0-6.9	0.1-10.2	99.2	4	98.7	100
			Surveillance	512	37	31-44	18-86	5.0	3.8-6.9	0.3-10.1	85.7	65	98.4	99.8
			Carboplatin × 1 AUC 7	188	37	31-45	16-73	3.4	2.8-4.0	0.2-6.0	96.1	7	99.2	100
			Other adjuvant chemotherapy†	11	39	33-50	28-55	4.3	3.2-5.9	1.5-7.8	100		90.9	100
2A	2A	2.5	Radiotherapy	29	33	30-40	25-65	5.7	3.7-6.9	2.4-9.5	88.7	3	100	100
			Chemotherapy	6	42	34-47	24-55	5.2	4.0-6.8	3.4-7.8	100		100	100
2B	2B	4.8	Chemotherapy	67	38	33-44	22-70	5.5	3.9-7.3	2.1-9.3	100		100	100
2C/2D	2C	3.0	Chemotherapy	42	39	34-49	17-75	5.5	4.4-7.3	0.1-9.6	85.1	6	95.1	97.6
3	3	1.7	Chemotherapy	24	38	34-45	20-64	5.5	4.3-7.8	2.1-9.4	95.8	1	91.3	100
4	3	1.4	Chemotherapy	20	43	36-52	22-71	3.4	2.4-5.3	0.7-8.3	84.2	3§	80.0	80.0
4	3 (good prognosis)‡		Chemotherapy	14	40	35-53	22-71	4.7	2.9-5.6	0.7-8.3	100§		92.9	92.9
4	3 (intermediate prognosis)‡		Chemotherapy	6	46	33-49	24-56	2.4	2.0-4.1	1.8-8.1	50	3	50.0	50.0
Other (n = 4)			See table 2		30	23-48	22-53	4.4	3.4-4.9	3.3-5.0		1	100	100

Abbreviations: CS, clinical stage; RMH, Royal Marsden Hospital [modified staging system]; AJCC, American Joint Committee on Cancer [staging system]; IQR, interquartile range; RFI, relapse-free interval (estimated using Kaplan-Meier survival curves); OS, overall survival (estimated using Kaplan-Meier survival curves); CSS, cause-specific survival (estimated using Kaplan-Meier survival curves).

*Doses of radiotherapy were 25.2 Gy in 82.3%, 27.0 Gy in 16.6%, and other in 1%.

†Regimens given were etoposide 100 mg/m^2 days 1 to 5 and cisplatin 20 mg/m^2 days 1 to 5 (EP) × 1 (n = 2), EP × 2 (n = 3), EP plus bleomycin 30,000 IU (30 mg) days 1, 5, and 15 (BEP) × 1 (n = 1), and carboplatin × 2 (n = 5).

‡Prognostic groups according to International Germ Cell Consensus Classification (IGCCC).

§One patient never went into remission.

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- First risk-adapted protocol in seminom
  - Stromal invasion rete testis
  - Maximum tumor diameter 4cm<
- Recommandations:
  - 0-1: Surveillance
  - 2: One course of adjuvant carboplatin AUC7

- 1118 patients
  - 423 surveillance
  - 690 carboplatin

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Table 4. Risk Factors According to Treatment and Risk Group

Treatment and risk group	No. of Patients	Median tumor size (mm), (IQR)	Stromal invasion rete testis (%)
Surveillance	404	26 (16-40)	16
0 risk factors[1]	269	22 (15-30)	0
1-2 risk factors[2]	135	45 (29-60)	53
Carboplatin AUC7	649	40 (25-60)	34
0 risk factors[1]	243	24 (15-34)	0
1-2 risk factors[2]	406	55 (45-67)	57

Abbreviations: IQR, interquartile range, AUC7, dosed at area under dose-time concentration curve x 7.
[1]Only patients with information on both tumor size and stromal invasion of the rete testis are registered as 0 risk factors
[2]Patients with minimum one risk factor

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Table 1. Treatment, Follow-up, Relapse and Survival

Treatment	No. of patients	Median follow-up, IQR (years)	Relapse rate (%)	Median time to relapse, range (years)	5-Year OS (%), 10-Year OS (%)	5-year CSS (%), 10-Year CSS (%)
All patients	1118	5.6 (4.4-7.0)	7.1	1.4 (0.2-6.9)	98.9, 97.8	100, 99.9
Surveillance	423	5.4 (4.4-6.3)	9	1.3 (0.4-6.9)	99.0, 96.6	100, 99.6
Carboplatin AUC7	690	5.7 (4.3, 7.3)	6.2	1.7 (0.2-6.5)	98.9, 98.5	100, 100
Other	5[1]	5.3 (4.1-6.7)	0	na.	80.0, 80.0	100, 100

Abbreviations: IQR, interquartile range; RFI, relapse-free interval (estimated using Kaplan-Meier survival curves); OS, overall survival; CSS, cause-specific survival (estimated using Kaplan-Meier survival curves); AUC7, dosed at area under dose-time concentration curve x 7.[1]Receiving two courses of carboplatin, n=5, dying of other cancer just after diagnosis of CSI seminoma, n=1

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Table 3. Cox proportional hazards survival regression for relapse in CS1 Seminoma, stratified by treatment

Tumor size	No. of Patients	HR	95% CI	
≤ 4cm	630	1.0		
> 4cm	351	2.7	1.7-4.7	$p<0.000$
Invasion rete testis				
Absent	715	1.0		
Present	266	1.9	1.2-3.2	$p=0.012$

Surveillance: 363 patients with 30 events, Carboplatin 547 patients with 38 events. Three patients censored before the earliest event in a stratum

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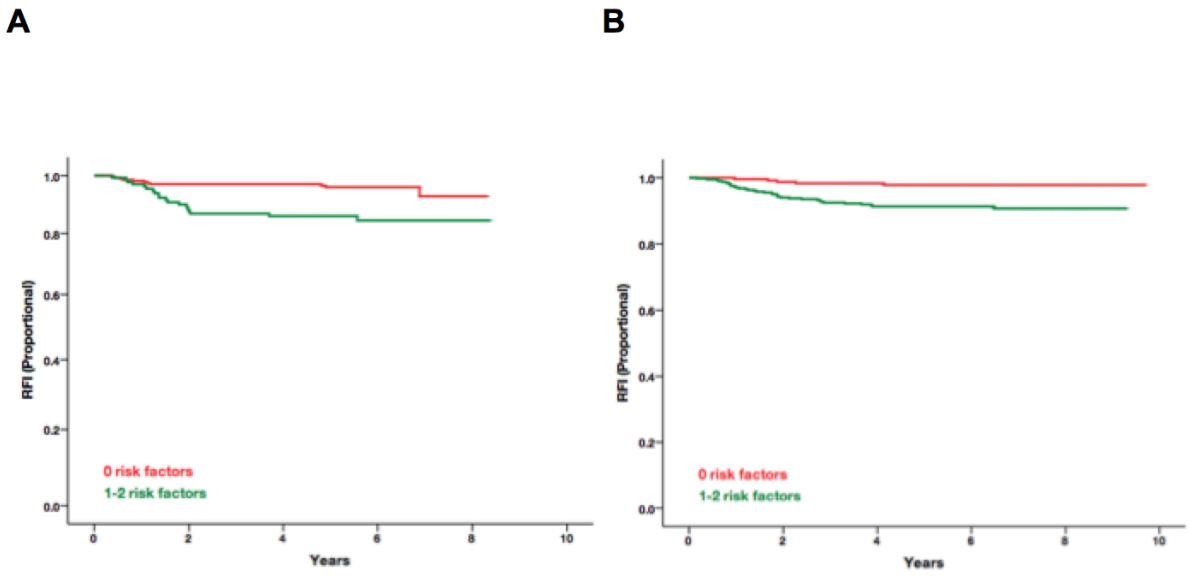

Fig 1. Kaplan-Meyer curves for relapse-free interval for (A) patients managed by surveillance (p=0.000), and (B) patients receiving one course of carboplatin AUC7 (p=0.001). Both compared according to the presence of risk factors.

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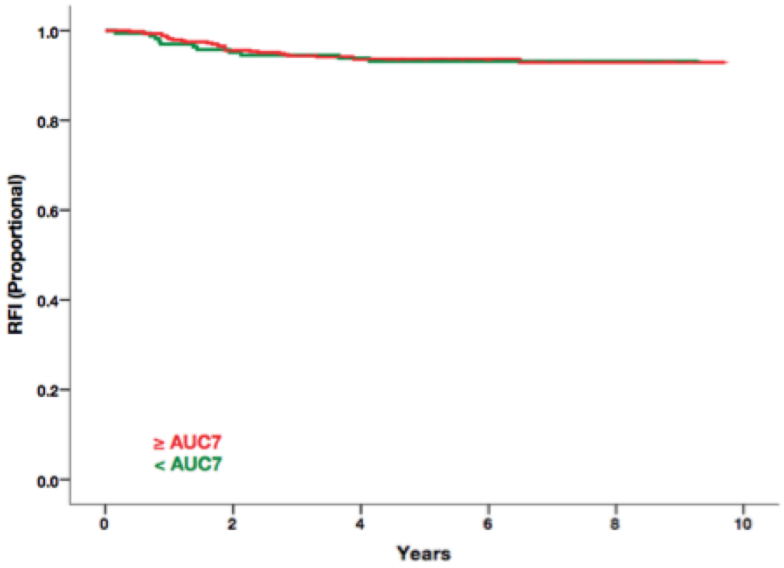
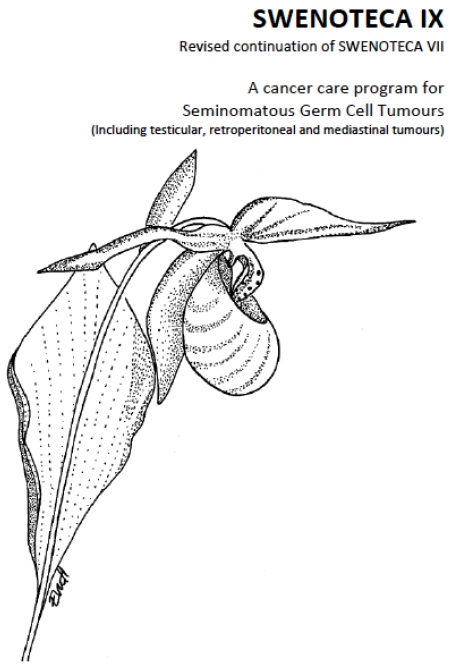


Fig 2. Kaplan-Meyer curves for relapse-free interval for patients receiving carboplatin, comparison of patients receiving a dose of ≥ AUC7 or a dose of < AUC7 (p=0.947).

SWENOTECA IX (Current)

SWENOTECA: Swedish & Norwegian Testicular Cancer group

- Risk adapted (stromal invasion rete testis, maximum tumor diameter 4cm<)
- CS I:
  - 0 risk factor: Surveillance
  - 1-2 risk factors: Carboplatin AUC7 or surveillance
- Metastatic:
  - BEP x 3
  - RT still a choice in CS IIA
- Relapse
  - Risk adapted according to IGCCCG-2



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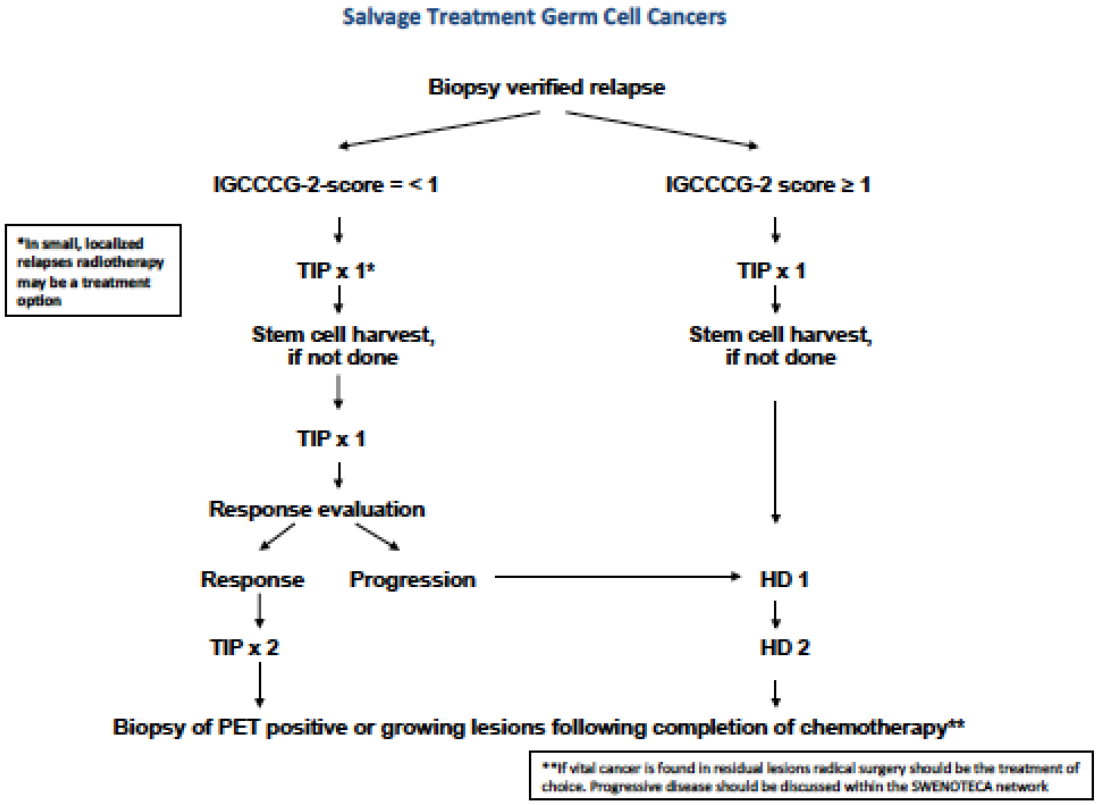
SWENOTECA IX | APPENDIX



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ABC-study

- A Randomized Phase III Study Comparing One Course of Adjuvant Bleomycin, Etoposide and Cisplatin (BEP) and One Course of Carboplatin AUC7 in Clinical Stage I Seminomatous Testicular Cancer, EUDRACT 2014-004075-23, NCT02341989

- 1-2 risk factors

ABC-study

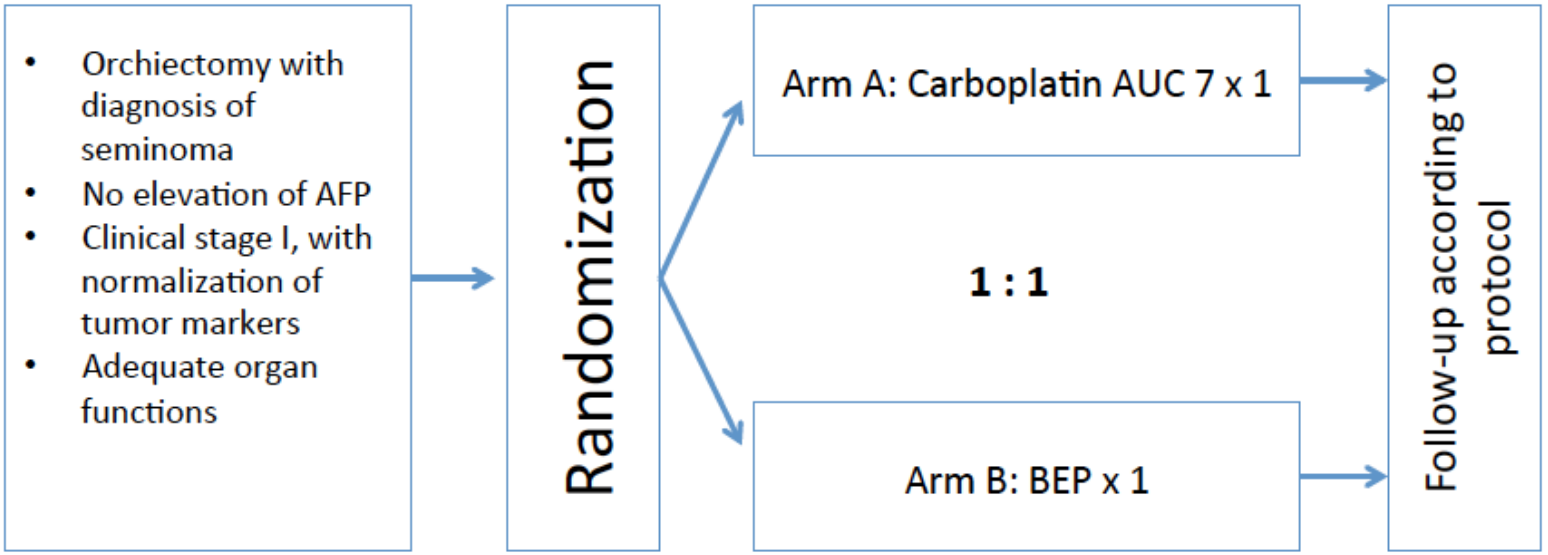


Figure 1. Flow chart – Trial design

RETROP

SWENOTECA – *RETROPSTUDIEN*

Ifyllt protokoll skickas **tidigast 90 dagar postoperativt** till:

Svenska patienter	**Norska patienter**
SWENOTECA sekretariatet	Kontor for klinisk kreftforskning
RCC Syd	Kreftavdelning
Scheelevägen 8	Haukeland Universitetssykehus
223 81 LUND	5021 BERGEN

Ansvarig urolog

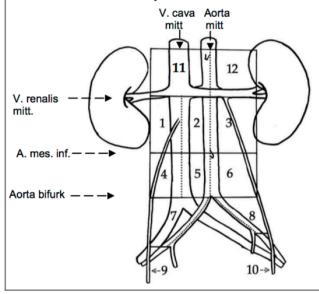
Sjukhus

Personnr |_|_|_|_|_|_|_|–|_|_|_|_| (år / mån / dag)

Namn

Studien innefattar alla svenska och norska män med icke-seminomatös testikelcancer som genomgått **retroperitoneal lymfkörtelutrymning** från och med den 1 sept 2007.

Det retroperitoneala rummets områdesindelning (numrerad)



1. Höger om cava -övre
2. Mellan cava och aorta -övre
3. Vänster om aorta -övre

4. Höger om cava -nedre
5. Mellan cava och aorta -nedre
6. Vänster om aorta -nedre

7. Iliaca communis -höger
8. Iliaca communis -vänster

9. V. spermatica -höger
10. V. spermatica -vänster

11. Suprahilärt -höger
12. Suprahilärt -vänster

Den retroperitoneala tumörutbredningen före kemoterapi och körtelutrymning

Före kemoterapi	
Område nr (enligt figur)	**Tumörstorlek*, mm**
1. ☐	
2. ☐	
3. ☐	
4. ☐	
5. ☐	
6. ☐	
7. ☐	
8. ☐	
9. ☐	
10. ☐	
11. ☐	
12. ☐	
Kommentar	

Före körtelutrymning	
Område nr (enligt figur)	**Tumörstorlek*, mm**
1. ☐	
2. ☐	
3. ☐	
4. ☐	
5. ☐	
6. ☐	
7. ☐	
8. ☐	
9. ☐	
10. ☐	
11. ☐	
12. ☐	
Kommentar	

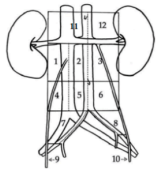
* största transversella diametern (mm)

Retroperitoneal lymfkörtelutrymning

Personnr |_|_|_|_|_|_|_|–|_|_|_|_| (år / mån / dag)

Omfattning av retroperitoneal lymfkörtelutrymning

Datum (år / mån / dag)	**Område nr (enligt figur)**											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Komplett utrymt												
Delvis utrymt												
Ej utrymt												



Blödning per operation ... ml

Operationstid min

Peroperativ preparathantering
Använd den numrerade områdesindelningen enl. ovan.
Varje utrymt område läggs i separat burk som märks med områdets siffra! (dvs en burk per utrymd station).

Nervsparande operation	**Nej**	**Ja**	**Delvis**	**Ej aktuellt**
Höger	☐	☐	☐	☐
Vänster	☐	☐	☐	☐

Komplikationer

Annan samtidig operation utöver körtelutrymningen ☐ Nej ☐ Ja

Om Ja, vilken typ av operation .....

Komplikationer ☐ Nej ☐ Ja

Om Ja, vilken **typ av komplikationer inom 30 dagar?**

Typ	**ICD 10 kod**	**Clavien grad ***	**Behandling**

Om ja, vilken **typ av komplikationer mellan 30-90 dagar?**

Typ	**ICD 10 kod**	**Clavien grad ***	**Behandling**

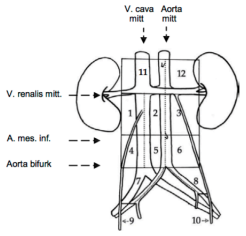
***Clavien system:**
Grad 1 peroral medicinering och "bedside" intervention
Grad 2 intravenös medicinering eller blodtransfusion
Grad 3 operativ, endoscopisk eller röntgenologisk intervention
3 a i lokalbedövning
3 b i generell anestesi
Grad 4 livshotande komplikation
Grad 5 död pga komplikation

Reoperation ☐ Nej ☐ Ja

Postoperativ vårdtid (antal nätter) .....

Kommentarer

Det retroperitoneala rummets områdesindelning (numrerad)



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8. Iliaca communis -vänster

9. V. spermatica -höger
10. V. spermatica -vänster

11. Suprahilärt -höger
12. Suprahilärt -vänster

Patologi

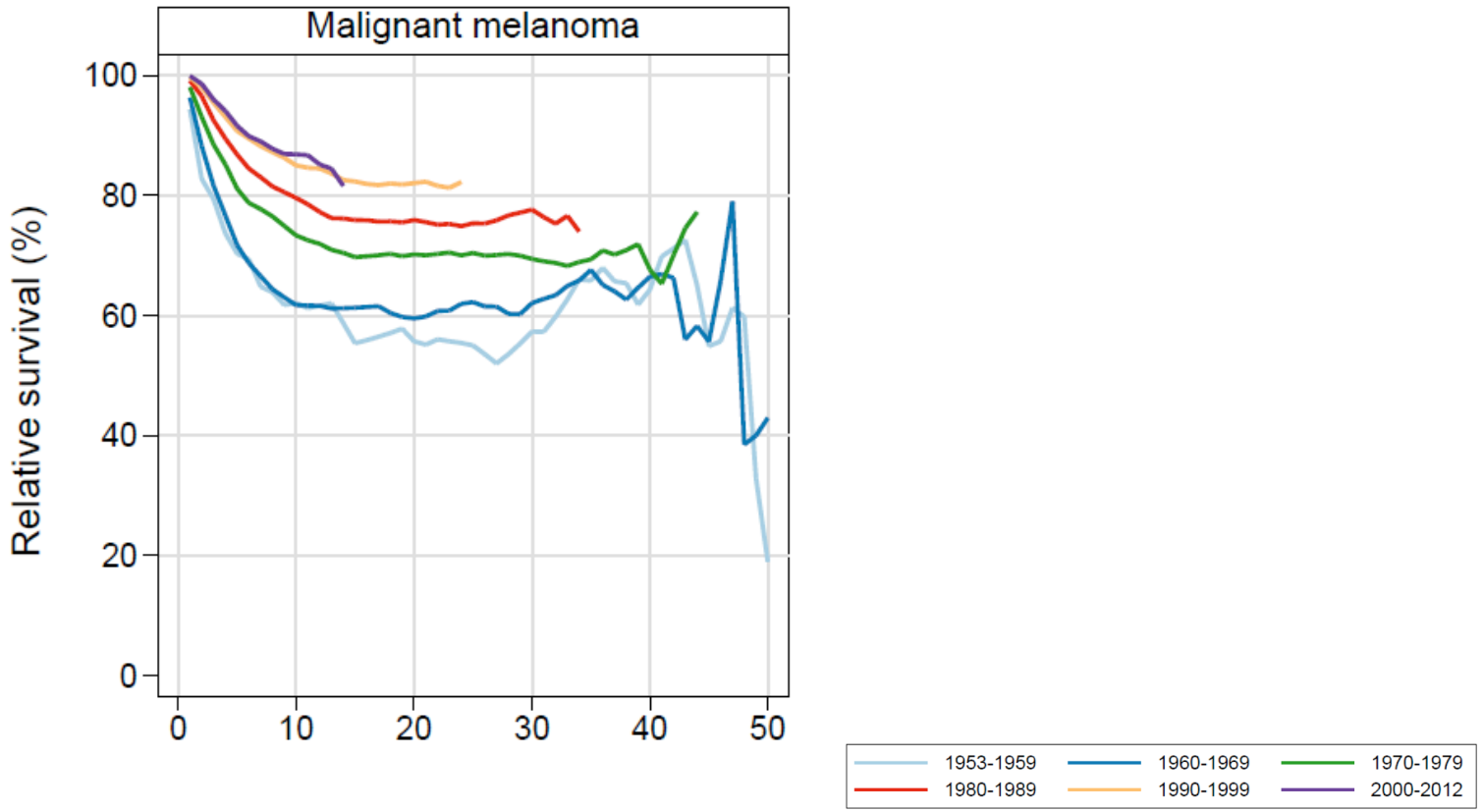
Datum |_|_|_|_|_|_|_|_| (år / mån / dag)

	PAD (antal körtlar)				
Område nr (enligt figur)	**Benignt**	**Teratom**	**Cancer**	**Totalt antal körtlar**	**Kommentar**
1. ☐					
2. ☐					
3. ☐					
4. ☐					
5. ☐					
6. ☐					
7. ☐					
8. ☐					
9. ☐					
10. ☐					
11. ☐					
12. ☐					
Totalt antal körtlar					

SWENOTECA

- Excellent outcomes comparable with large tertiary centres
- Community based
- Continuous focus on high quality care
- Constant evaluation and changing of management programs
- Role model for multidisciplinary approach
- An arena to discuss challenging patients
- Annual meeting open to all

Long term toxicity, relative survival



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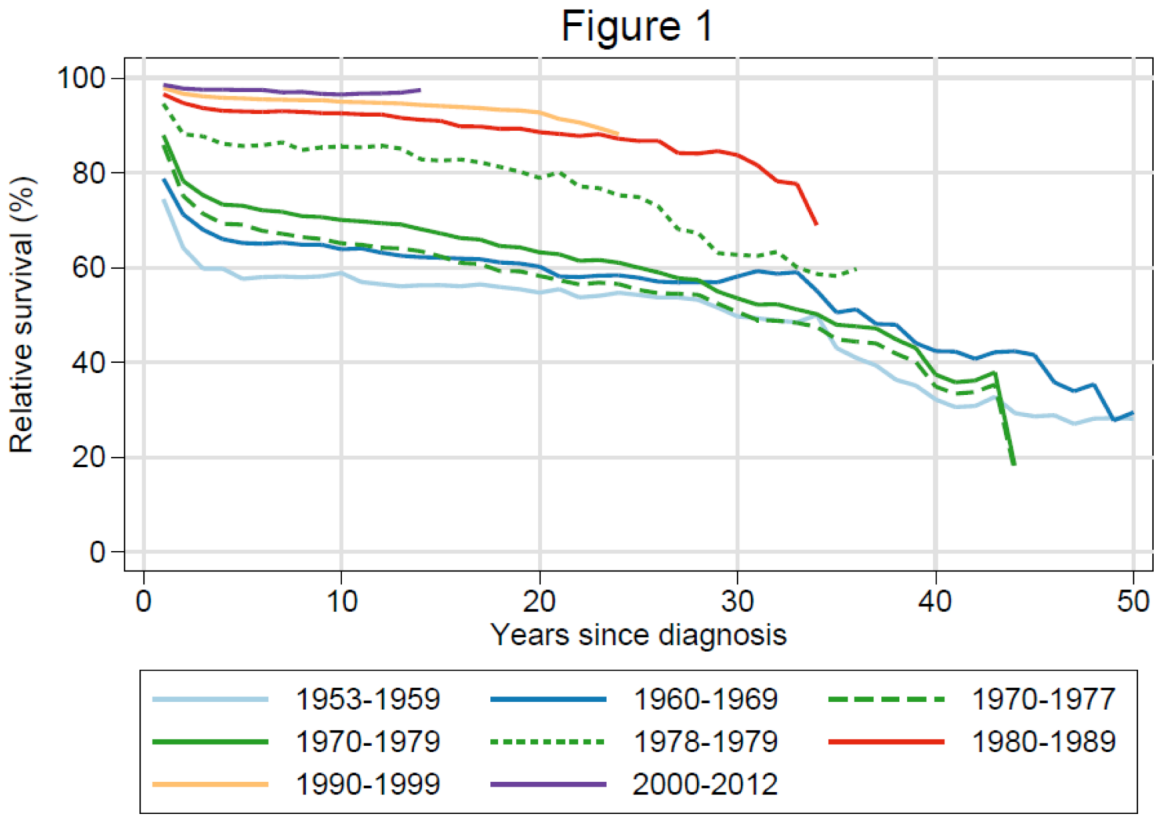
Long term toxicity, relative survival



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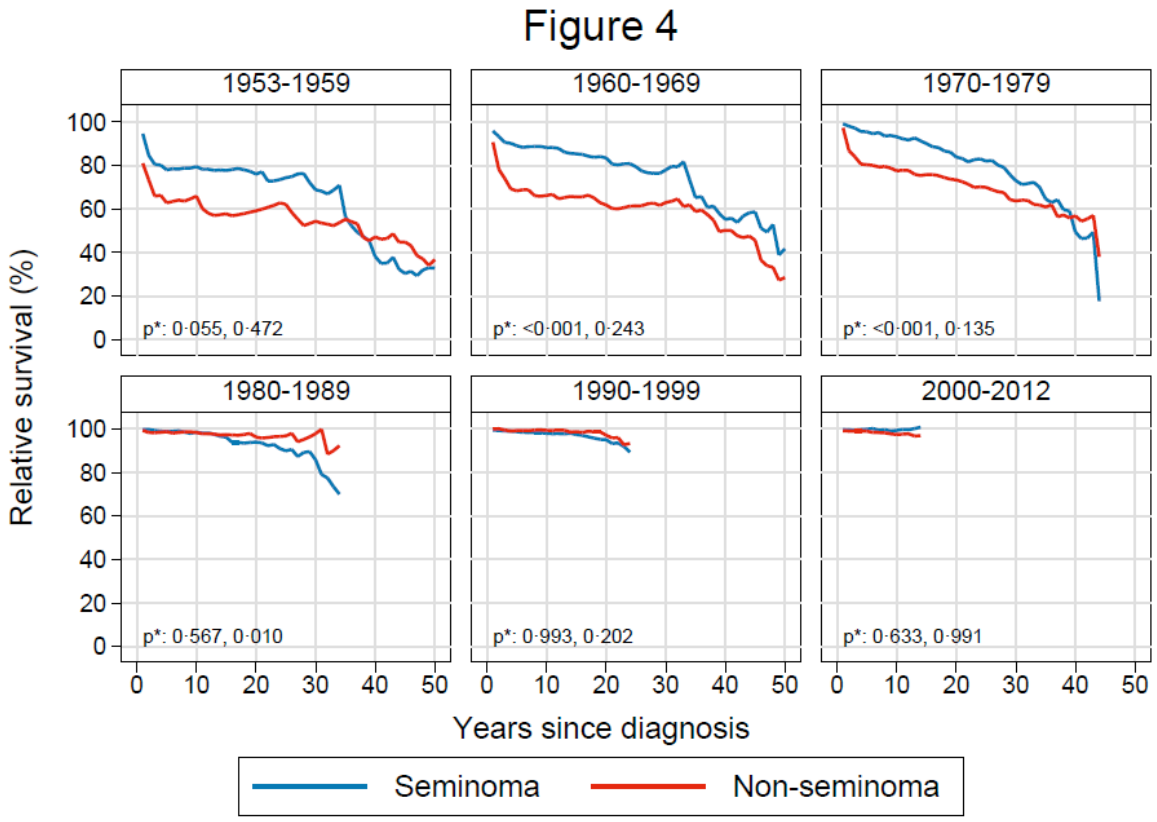
Long term toxicity, relative survival, CS I



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Questions

- Do you start off planning to give all 12 doses of bleomycin to men with high or intermediate risk metastatic non-seminoma? What do you base the decision of discontinuing the drug on – lung functioning tests (how big a decline?), clinical symptoms (severity?), something else?
  - No: Max 300 000 IE (10 doses)
  - In case of suspected bleomycin toxicity PEI instead of BEP

Questions

- If there is no clinical trial available or the patient doesn't fulfill the inclusion criteria, which regimen do you administer to high risk patients? Does it vary based on clinical factors? Is there an open clinical trial for these patients running in Scandinavia, Dr. Tandstad?
  - BEP x 4, with two intensification steps based on marker decline:
    I: PEI (Poor prognosis, marker only)
    I: TIP (Poor prognosis, non-visceral metastasis)
    II: HD

Questions

- Do you treat patient with chorion carcinoma differently from other patient groups?
  - No: BEP
  - If brain metastasis: PEI

Questions

- Would you recommend surgery of the retroperitoneum and / or lungs/ mediastinum if there is no possibility to radically operate the residual tumours in other organs in patients with metastatic non-seminoma?
  - Yes

Questions

- We just had a 40 y old patient with high risk non-seminoma (markers + liver + bone) sent to us, who had received BEP in the first line with initial PR but PD at the end of 4 courses and TaxIP x 3 in second line with the same result. Which regimen would you choose for third line and would you go for an autologous transplant, if he responds? Or would you declare his cancer platin-resistant and opt for palliative therapy?
  - No. HD x 2.

Questions

- What to do you with patient with brain metastasis either at diagnoses or at relapse? Could you give us an idea how you approach this dilemma?

Flow sheet 6

SWENOTECA VIII
Treatment of patients with brain metastases at diagnosis

If resectable brain metastasis and a short delay of start of chemotherapy is possible, consider primary brain surgery

Chemotherapy according to poor-prognosis with extrapulm visceral metastases except that PEI is given instead of BEP (ifosfamide better penetration to CNS than bleomycin)

↓

Systemic extracerebral disease under control

CR brain	PR brain		PD brain
No further therapy to brain	If resectable surgery → If vital cancer wb RT	If not resectable, radiotherapy	Radiotherapy wbr (if the tumour is a ch carcinoma, consider POMB-ACE CHT instead of RT)

Wb RT=whole brain radiotherapy, 40 Gy, fraction dose 1.8 Gy. Consider boost to tumour up to max 54 Gy

Page 60

Flow sheet 7

SWENOTECA VIII
Treatment of patients with brain metastases at relapse after CR

Patients treated with cisplatin-based chemotherapy and obtained complete remission

Brain as only site		**Brain relapse as part of systemic relapse**
Resectable	Not resectable	
Surgery followed by wb RT	Wb RT 40 Gy. Consider boost to tumour up to max 54 Gy	Salvage chemotherapy according to protocol. Treatment of brain depends on response to salvage chemotherapy

Wb RT =whole brain radiotherapy, 40 Gy, fraction dose 1.8 Gy,

Questions

- A young man came to us with chorion carcinoma. At diagnoses he had one brain metastases that caused the paralysis of his right hand and was deemed inoperable by the neurosurgeon. He was in CR after BEP x 4 and we were starting a course of stereotactic radiotherapy by which time – three weeks - he presented with multiple brain metastases at the ER. Have you any advice as what could have been done differently?
  - We would have started PEI. In case of CR in CNS we would not have given RT.

Questions

- We have a mentally disabled patient whom we dare not operate because fears for his postoperative co-operation, or rather, lack of it judged from how he acted during chemotherapy. Would you use radiotherapy instead of surgery for single patients with metastatic pure seminoma with large residual tumours or does chemotherapy render the residual tumour cells resistant to radiation?
  - PET-CT if residual tumor over 3cm (minimum 12 weeks after chemo)
  - PET +: Biopsy
  - PET -: Observation
  - Observation an option as long as residual mass is declining
  - If candidate for RT, he should be a candidate for surgery