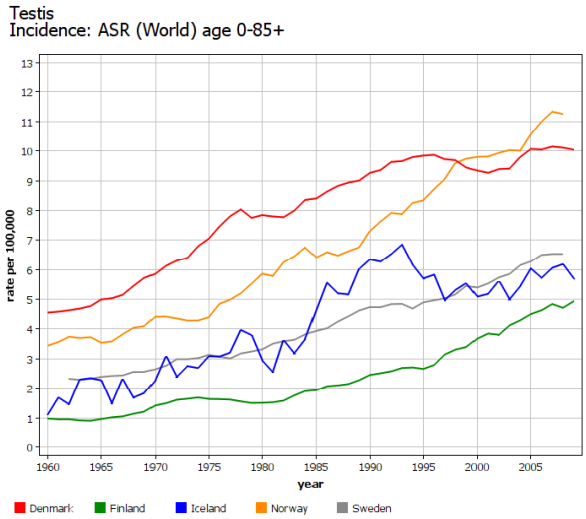
Kivessyövän hoidossa tapahtuu

S. Jyrkkiö, Tyks

Onkologiapäivät 30.8.2014

Kivessyöpä yleistyy



Nordcan database/Ylönen O.

reviews

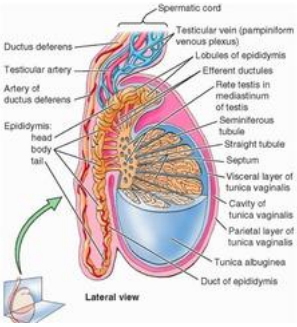
Annals of Oncology 24: 878–888, 2013
doi:10.1093/annonc/mds579
Published online 14 November 2012

Maintaining success, reducing treatment burden, focusing on survivorship: highlights from the third European consensus conference on diagnosis and treatment of germ-cell cancer

ST I kivessyöpä: seuranta tai adj hoito?

Table 2. Strategies in clinical stage I seminoma and non-seminoma

Seminoma	
Risk factors for occult metastases:[a]	Tumor size ≥4 cm Invasion of rete testis
Treatment options:	Surveillance (preferred in low risk patients) One cycle carboplatin AUC 7 Adjuvant paraaortic radiation 20 Gy[b]
Non-seminoma	
Risk factors for occult metastases:	Vascular or lymphatic invasion
Treatment options:	Surveillance (preferred in low risk patients) One adjuvant cycle BEP Two adjuvant cycles BEP Primary RPLND (rarely indicated)[c]

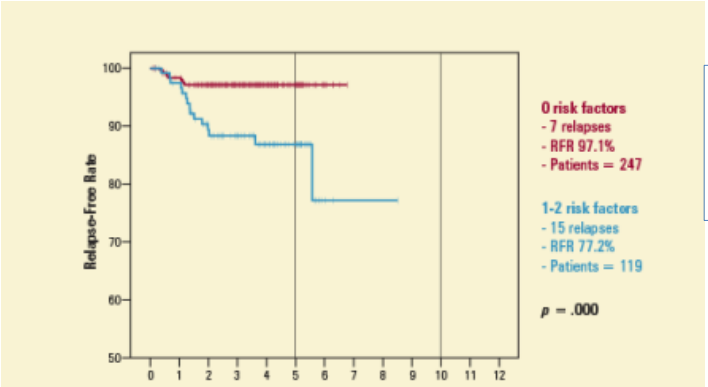


Seminoma ST I
SWENOTECA tulokset

- V 2007-2010 prospektiivinen tutkimus
- Potilaille tarjottiin seurantaa tai single karbopl.
- Seurantaa suositeltiin, jos riskitekijöitä 0-1
  => 50 % halusi adjuvanttihoidon
- Karboplatiinia suositeltiin, jos 2 riskitekijää
  => 90 % sai hoidon
- Seurantaryhmässä N=391 (FU 3,6 v)
- Karbopl. hoidetussa ryhmässä N=447 (5,2 v)

Tandstad ym. SWENOTECA, ASCO 2014 #4508

Seminoma: pelkkä seuranta, riskitekijöiden merkitys



0 riskitekijää
Relapseja **3 %**

1-2 riskitekijää
Relapseja **23 %**

Riskitekijät:
- tuumori > 4 cm
- Rete testis inv.

Tandstad ym. ASCO 2014 Abstr. #4508

ST I Seminooma, karbopl annettu

- Karbopl. Hoidon sai N=669
- Relapseja N= 36 RFR 93,8 %
- Riskitekijät 0 => RFR 97,7 % (N=236)
- Riskitekijät 1-2 => RFR 90,6 % (N=337)

Relapseja:
2 %
9 %

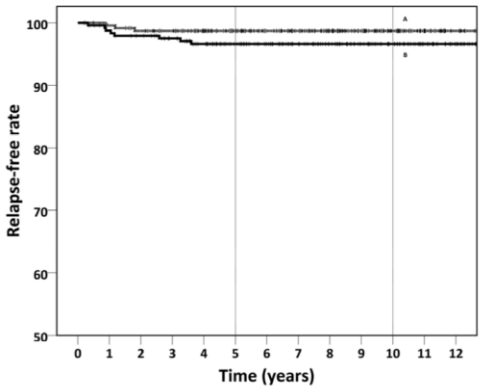
- *”We recommend patient autonomy”*
- ***Jos ei riskitekijöitä => adj hoidosta ei hyötyä***

Annals of Oncology Advance Access published August 11, 2014

1

One Course of Adjuvant BEP in Clinical Stage I Nonseminoma

Mature and Expanded Results from the SWENOTECA group



N=517, FU 7,9 v

A= LVI – relapseja 1,6 %
B= LVI + relapseja 3,2 %
OS 100 %

Myöhäisin relapsi 3,3 v

A N= 255
B N=258

HAUGNES, STEPHENSON, AND FELDMAN

Beyond Stage I Germ Cell Tumors: Current Status Regarding Treatment and Long-Term Toxicities

Hege Sagstuen Haugnes, MD, PhD, Andrew J. Stephenson MD, FRCSC, FACS, and Darren Richard Feldman, MD

Levinneen kivessyövän hoito

20 – 40 % kaikista potilaista tarvitsee hoitoa levinneen taudin takia (prim levinneet tai uusiutuman takia)

e180 2014 ASCO EDUCATIONAL BOOK | asco.org/edbook

International Prognostic System for advanced germ cell cancer

	Good	Intermediate	Poor
Seminona	Ei NPVM	NPVM	N/A
Nonseminoma	Testis tai RP ja Ei NPVM ja S0 tai S1	Testis tai RP ja Ei NPVM ja S2	Prim. Mediastinum tai NPVM tai S3
5 v PFS	88 %	75 %	41 %
5 v OS	91 %	79 %	48 %

NPVM = nonpulmonary visceral metastases
RP = retroperitoneal
S1 LD < 1,5 x N ja HCG < 5000 ja AFP < 1000
S2 LD 1,5-10 x N tai HCG 5000-50000 tai AFP 1000-10000
S3 LD > 10xN tai HCG>50000 tai AFP >10000

JCO 1997;15:594

Huonon ennusteen potilaiden hoito: onko 4xBEP:lle vaihtoehtoa?

- BEP vs VIP: yhtä hyvät tulokset, mutta VIP enemmän toksisuutta [1]
- EORTC 30983: BEP vs T-BEP [2]
  - ITT analysis 3 y PFS 71 vs 79 %, ns
  - OS ns
- GETUG-13: BEP vs BEPx1 => DIR (+paklitakseli, oksaalipl) [3,4]
  - 3 y PFS 48 vs 59 % p=0,05; OS ns
  - Ei elinaikaetua, vaikea ja toksinen hoitoprotokolla

1. Cancer 2003;97:1869
2. JCO 2012;30:792
3. JCO 2004;22:3868
4. JCO 2013;31:suppl #4500

Rekrytoivat tutkimukset: intermediate/poor risk, first line

- Australia: BEP vs accelerated BEP (sykli 14 d)
- US: BEP vs TIP

Paclitaxel, Ifosfamide and Cisplatin (TIP) Versus Bleomycin, Etoposide and Cisplatin (BEP) for Patients With Previously Untreated Intermediate- and Poor-risk Germ Cell Tumors. ClinicalTrials.gov Identifier: NCT01873326. Est completion 2018

Uusiutuneen/refraktaarin kivessyövän hoito

20-30 % levinneen kivessyövän sairastaneista saa taudin uusiutuman

VOLUME 28 · NUMBER 33 · NOVEMBER 20 2010

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prognostic Factors in Patients With Metastatic Germ Cell Tumors Who Experienced Treatment Failure With Cisplatin-Based First-Line Chemotherapy

The International Prognostic Factors Study Group

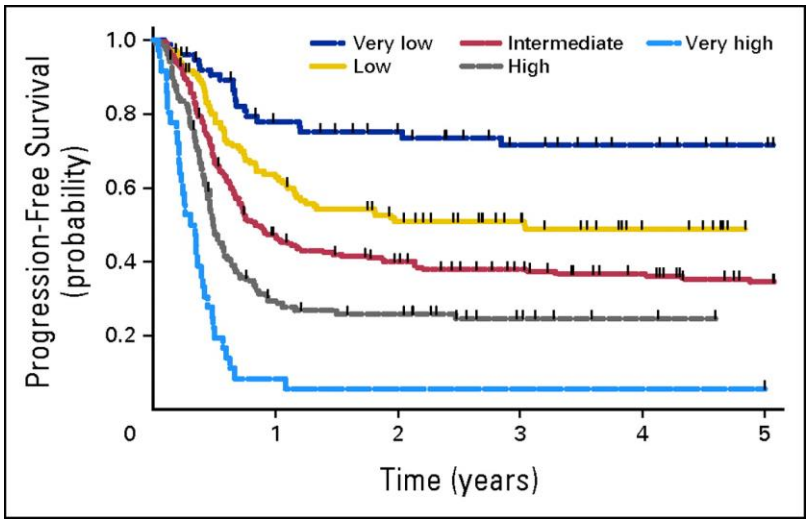
- N=1984 patients with relapsed or refractrory GCT
- 38 centers
- 13 countries

Table 4. Prognostic Score for Patients With Nonseminoma and Seminoma

Parameter	Score Points 0	1	2	3	Score
Primary site	Gonadal	Extragonadal	—	Mediastinal nonseminoma	
Prior response	CR/PRm−	PRm+/SD	PD	—	
PFI, months	> 3	≤ 3	—	—	
AFP salvage	Normal	≤ 1,000	> 1,000	—	
HCG salvage	≤ 1,000	> 1,000	—	—	
LBB	No	Yes	—	—	
Score sum (values from 0 to 10)					
Regroup score sum into categories: (0) = 0; (1 or 2) = 1; (3 or 4) = 2; (5 or more) = 3					
Add histology score points: pure seminoma = −1; nonseminoma or mixed tumors = 0					
Final prognostic score (−1 = very low risk; 0 = low risk; 1 = intermediate risk; 2 = high risk; 3 = very high risk)					

Abbreviations: CR, complete remission; PRm−, partial remission, negative markers; PRm+, partial remission, positive markers; SD, stable disease; PD, progressive disease; PFI, progression-free interval; AFP, alpha fetoprotein; HCG, human chorionic gonadotrophin; LBB, liver, bone, brain metastases.

Progression-free survival according to prognostic category (validation set plus patients with seminoma).



The International Prognostic Factors Study Group JCO 2010;28:4906-4911

Uusiutuneen kivessyövän hoito

- TIP CR 70 %, at 69 m CR:ssä 63 % (N=46) [1]
- VIP CR 50 %, joista puolet pitkäkestoisia
- NY Sloan Kettering hoitoprotokolla: TIP -/+ HDT(TI-CE)+ASCT jos huono/hidas hoitovaste TIP:lle
- Randomoitu trial: HDTx1 ei hyötyä[2]
- Tai kaikille HDT+ASCT??[3]

1. JCO 2005;23:6549
2. Ann Oncol 2005;16:1152
3. NEJM 2007;357:340

The NEW ENGLAND JOURNAL of MEDICINE
N Engl J Med 2007;357:340-8.

ORIGINAL ARTICLE

High-Dose Chemotherapy and Stem-Cell Rescue for Metastatic Germ-Cell Tumors

Lawrence H. Einhorn, M.D., Stephen D. Williams, M.D., Amy Chamness, B.A., Mary J. Brames, R.N., Susan M. Perkins, Ph.D., and Rafat Abonour, M.D.

- Retrospective review N=184
- Induktiohoito VIP (N=110)
- 2 x HDT + ASCT
- HDT 1-3 d:
  Carboplatin 700 mg/m^2
  Etoposide 750 mg/m^2
- 3 deaths
- 3 leukemiaa

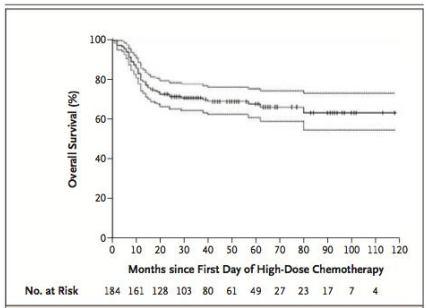


Figure 1. Kaplan–Meier Estimates of Overall Survival.
The top and bottom lines show the 95% confidence interval.

VOLUME 29 · NUMBER 16 · JUNE 1 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Conventional-Dose Versus High-Dose Chemotherapy As First Salvage Treatment in Male Patients With Metastatic Germ Cell Tumors: Evidence From a Large International Database

Anja Lorch, Caroline Bascoul-Mollevi, Andrew Kramar, Lawrence Einhorn, Andrea Necchi, Christophe Massard, Ugo De Giorgi, Aude Fléchon, Kim Margolin, Jean-Pierre Lotz, Jose Ramon Germà-Lluch, Thomas Powles, Christian Kollmannsberger, and Jörg Beyer

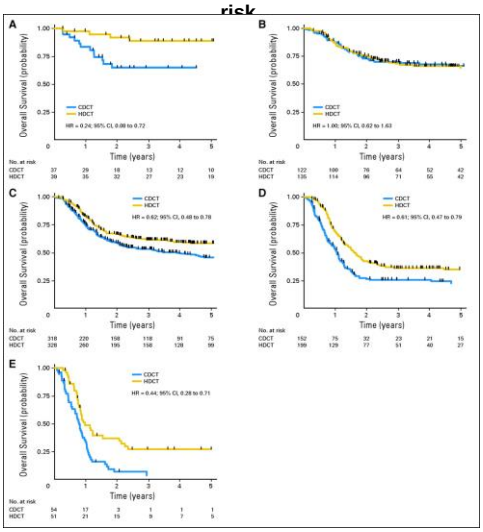
CDCT N=773 (49 %)
HDCT N=821 (51 %)

CDCT	N	5 y OS rate (%)
TIP	90	46,3 n.s.
VIP/PEI	285	43,2
VeIP	188	34,0
Muu	210	41,4

	N	5 v OS (%)
CDCT	773	40,8
HDCT	821	**53,2** *
HDCT single	408	46,3
HDCT seq	413	**60,6** *
HD CE	301	**62,0** *
HD CEI	95	34,9
HD CET	102	43,9
HD CEC	212	55,9
Muu	111	49,4

* $P < 0,001$

Overall survival and corresponding hazard ratios (HR) in each of the five prognostic categories: (A) very low risk; (B) low risk; (C) intermediate risk; (D) high risk; (E) very high risk



Lorch A et al. JCO 2011;29:2178-2184

JOURNAL OF CLINICAL ONCOLOGY ASCO

TIGER trial

TIP (ARM A)

Cycles 1-4 (q21d)

- *Paclitaxel 250mg/m2 IV over 24 hrs (d1)*
- *Ifosfamide 1500mg/m2 IV + mesna support (d2-5)*
- *Cisplatin 25mg/m2 IV (d2-5)*
- *Peg-G-CSF 6mg SQ (d6) or G-CSF 5mcg/kg (d7-13)*

Eligibility

- *Histologically-confirmed GCT*
- *PD following 1st-line chemo*
- *Prior treatment included ≥3 but ≤6 cycles of cisplatin-based chemo*
- *Adequate organ function for HDCT*
- *Any primary site*

TI-CE (ARM B)

Cycles 1-2 (q14d)

- *Paclitaxel 250mg/m^2 IV over 24hrs (d1)*
- *Ifosfamide 2000mg/m^2 IV + mesna support (d2-4)*
- *G-CSF 10mcg/kg/d (d4-14)**
- *Stem cell collection (d11-14)**

Cycles 3-5 (q21d)

- *Carboplatin AUC=8 IV (d1-3)*
- *Etoposide 400mg/m2 IV (d1-3)*
- *Stem cell infusion*
- *G-CSF 10mcg/kg/d (d3-ANCR) or Peg-G-CSF 6mg SQ once (d5)*

Journal of Cancer

2011; 2: 374-377

Seurantakuvaukset

- Ei rutiini TT-tutkimuksia 5 v jälkeen
- MRI?

EAU Guidelines on Testicular Cancer: 2011 Update

Peter Albers[a,], Walter Albrecht[b], Ferran Algaba[c], Carsten Bokemeyer[d], Gabriella Cohn-Cedermark[e], Karim Fizazi[f], Alan Horwich[g], Maria Pilar Laguna[h]*

EUROPEAN UROLOGY 60 (2011) 304–319

Patterns of management and surveillance imaging amongst medical oncologists in Australia for stage I testicular cancer

Peter Grimison[1,2], Baerin Houghton[1,3], Mark Chatfield[1,3], Guy C. Toner[1,6,7], Ian D. Davis[1,8], Jarad Martin[1,4], Elizabeth Hovey[1,5] and Martin R. Stockler[1,2,3]

[1]Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group Ltd, [2]Sydney Cancer Centre and University of Sydney, [3]NHMRC Clinical Trials Centre, University of Sydney, Sydney, [4]Calvary Mater Newcastle, Waratah, [5]Prince of Wales Hospital, Randwick, NSW, [6]Peter MacCallum Cancer Institute, [7]University of Melbourne, [8]Ludwig Institute for Cancer Research, Joint Ludwig-Austin Oncology Unit, Austin Health, Melbourne, Vic., Australia

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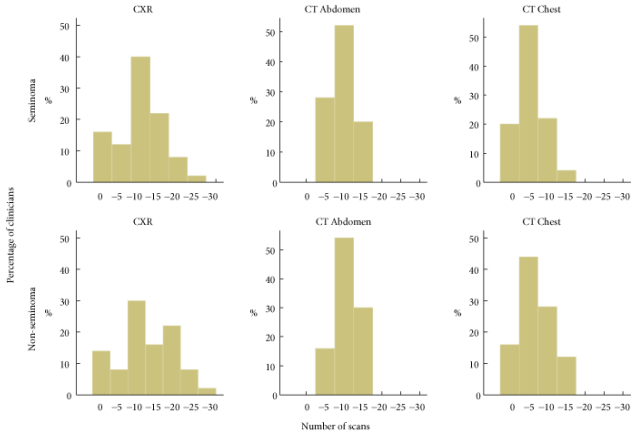
Table 4 Consensus recommendations for number of imaging procedures during 5 years of surveillance.

Group (Year published)	Seminoma			Non-seminoma		
	Chest X-ray	CT Chest	CT Abdomen	Chest X-ray	CT Chest	CT Abdomen
MRC 1992 [25]	NS	NS	NS	22	4–8	4–8
Princess Margaret 2007 [34]	10	0	11 (also pelvis)	NS	NS	NS
Marsden 2008 [12]	7	0	7	18	0	3
ESMO 2010 [18,19]	7	0	7	18	0	3
European Association of Urology 2011 [16]	4	0	4 (also pelvis)	4	0	2 (also pelvis)
Swiss-German group 2011 [38]	6	0	4†	15	0	2†
NCCN 2012 [14]	NS	NS	7–10 (also pelvis)	21–27	0	8–12 (also pelvis)

EMSO, European Society of Medical Onocolgy, MRC, Medical Research Council; NCCN, National Comprehensive Cancer Network. †Also ultrasonography of the abdomen. NS, not specified.

Patterns of management and surveillance imaging amongst medical oncologists in Australia for stage I testicular cancer



BJU International
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http://onlinelibrary.wiley.com/doi/10.1111/bju.12221/full#bju12221-fig-0001

Magnetic Resonance Imaging and Computed Tomography in Patients With Stage I Seminoma of the Testicle

Tavoite N=660, suljetaan Dec 2016

- I: Abomen CT 6, 12, 18, 24 36, 48, 60 m
- II: Abdomen CT 6, 18, 36 m
- III: Abdomen MRI 6, 12, 18, 24 36, 48, 60 m
- IV: Abdomen MRI 6, 18, 36 m

ClinicalTrials.gov Identifier:
NCT00589537

Myöhäishaitat

- Fertiliteetti säilynyt n 70 %:lla
- Jälkeläiset terveitä
- 11-35 % hypogonadismi (S-testo < 8 nmol/l)
- 2-3 x riski kardiovaskulaarisairauksiin, kumulatiivinen riski 20 v 18 %
- Raynaudin oire voi olla merkki lis riskistä
- Metabolinen syndrooma 25 %:lla 5 v kuluttua
- Keuhko-, munuais ja ototoksisuus
- Sekundaarimaligniteettien riski x 2
- Psykososiaaliset oireet