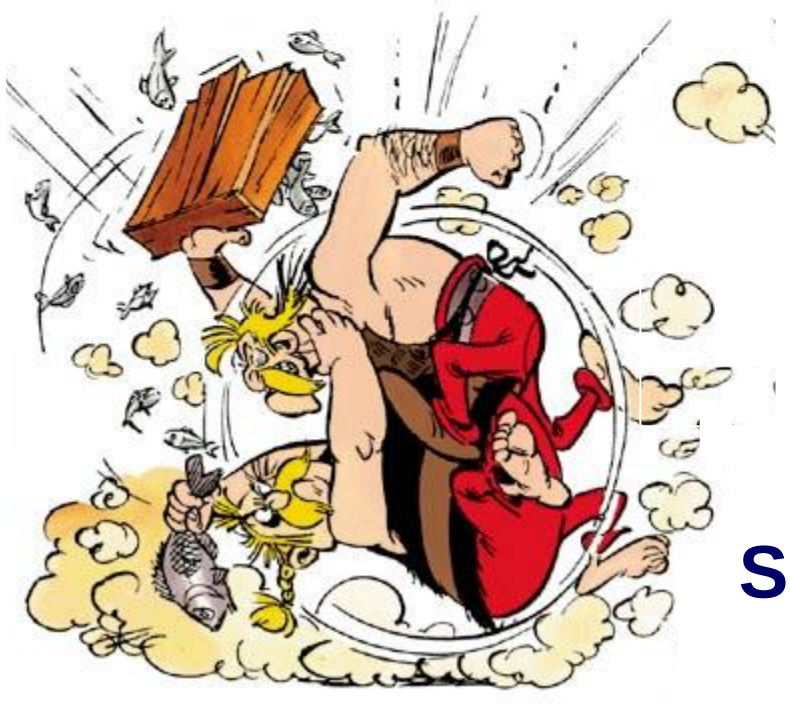
Welcome to the debate
Salvage Treatment in Testis Cancer



The expert: Jörg Beyer
University Zürich
Switzerland
joerg.beyer@usz.ch

Special Guests: ESMO, EAU, NCCN
European Consensus

Estimated Incidence Rates Testis Cancer

~ 4000 new cases
in Germany per year

Rosen A, Jayram G, Drazer M, Eggener SE. Global trends in testicular cancer incidence and mortality. Eur Urol. 2011 Aug;60(2):374-9. Epub 2011 May 17.

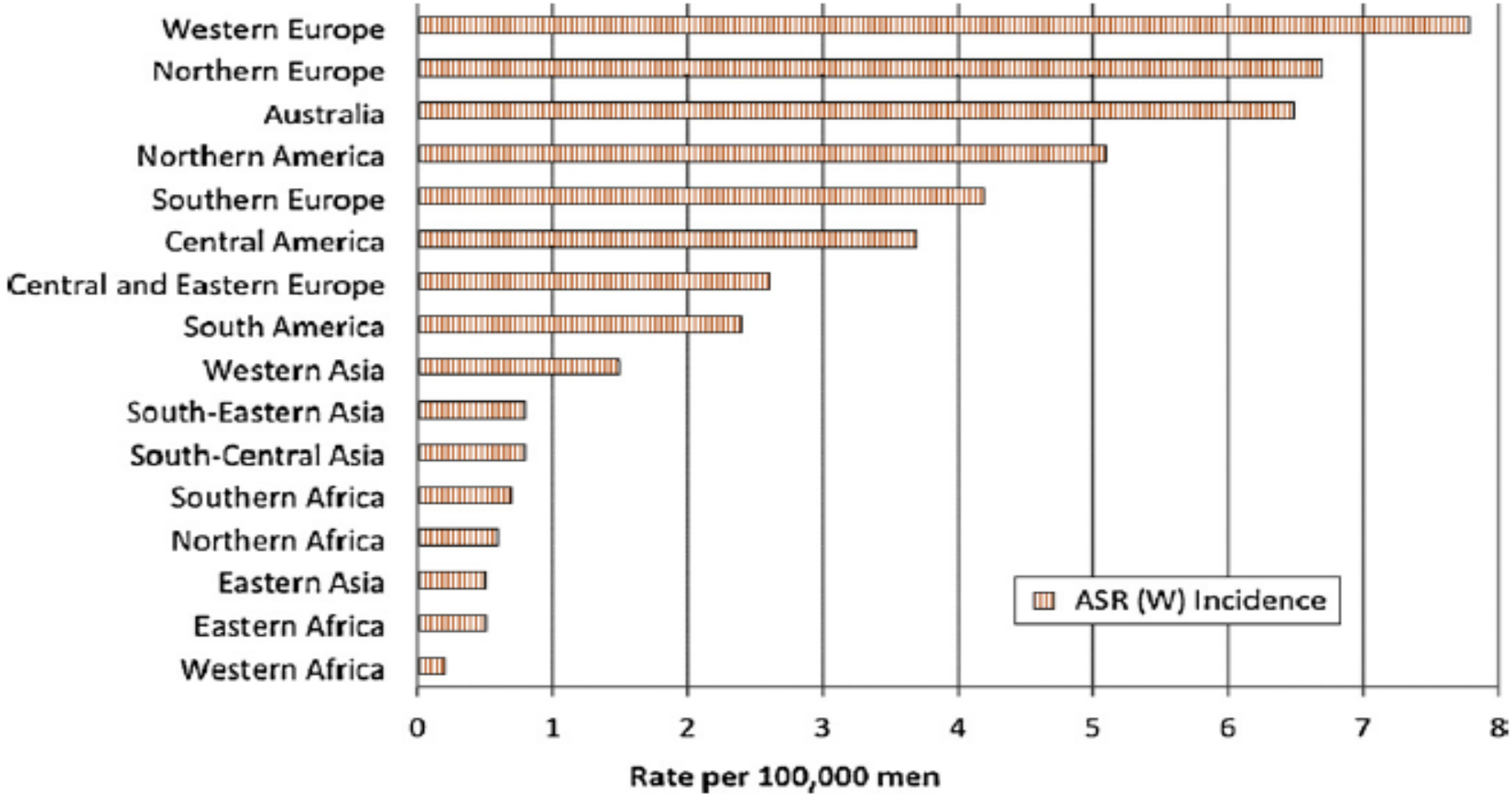


Fig. 1 – Incidence rates of testicular cancer (per 100 000) age standardized to the world population.

Stage Distribution & Outcome Germ-cell Cancer Germany

~ 4000 new patients
~ 120 deaths

Stage	Frequency	No pts	Cures	Relapses
Stage I	60%	2400	99%	20 pts
Metastatic				
good	56%	900	90%	90 pts
intermediate	28%	400	78%	80 pts
poor	16%	300	45%	160 pts

3-4 x BEP every 21 days

Conventional-dose chemotherapy regimens

Therapieschema		Referenz	Anwendung		Intervall (Tage)	Zyklus-zahl
			Dosis	Dauer (Tage)		
PEB	Cisplatin	[23]	20 mg/m^2	1–5	21 [a]	3–4 [b, c]
	Etoposid		100 mg/m^2	1–5		
	Bleomycin		30 mg	abs. 1, 8, 15		
PE	Cisplatin	[22]	20 mg/m^2	1–5	21 [a]	4 [b]
	Etoposid		100 mg/m^2	1–5		
PEI	Cisplatin	[18]	20 mg/m^2	1–5	21 [a]	3–4 [b, c]
	Etoposid		75 mg/m^2	1–5		
	Ifosfamid		1,2 g/m^2	1–5		

Surival after first-treatment

	Risk Groups			
(299 Patients)	good	inter-mediate	poor	all
1977-1986	95%	74%	37%	76%
1987-1996	94%	87%	66%	88%

Sonneveld et al., Cancer 2001, 91: 1304

The problem:

How should we treat patients who relapse after 3-4 cycles first-line treatment ?

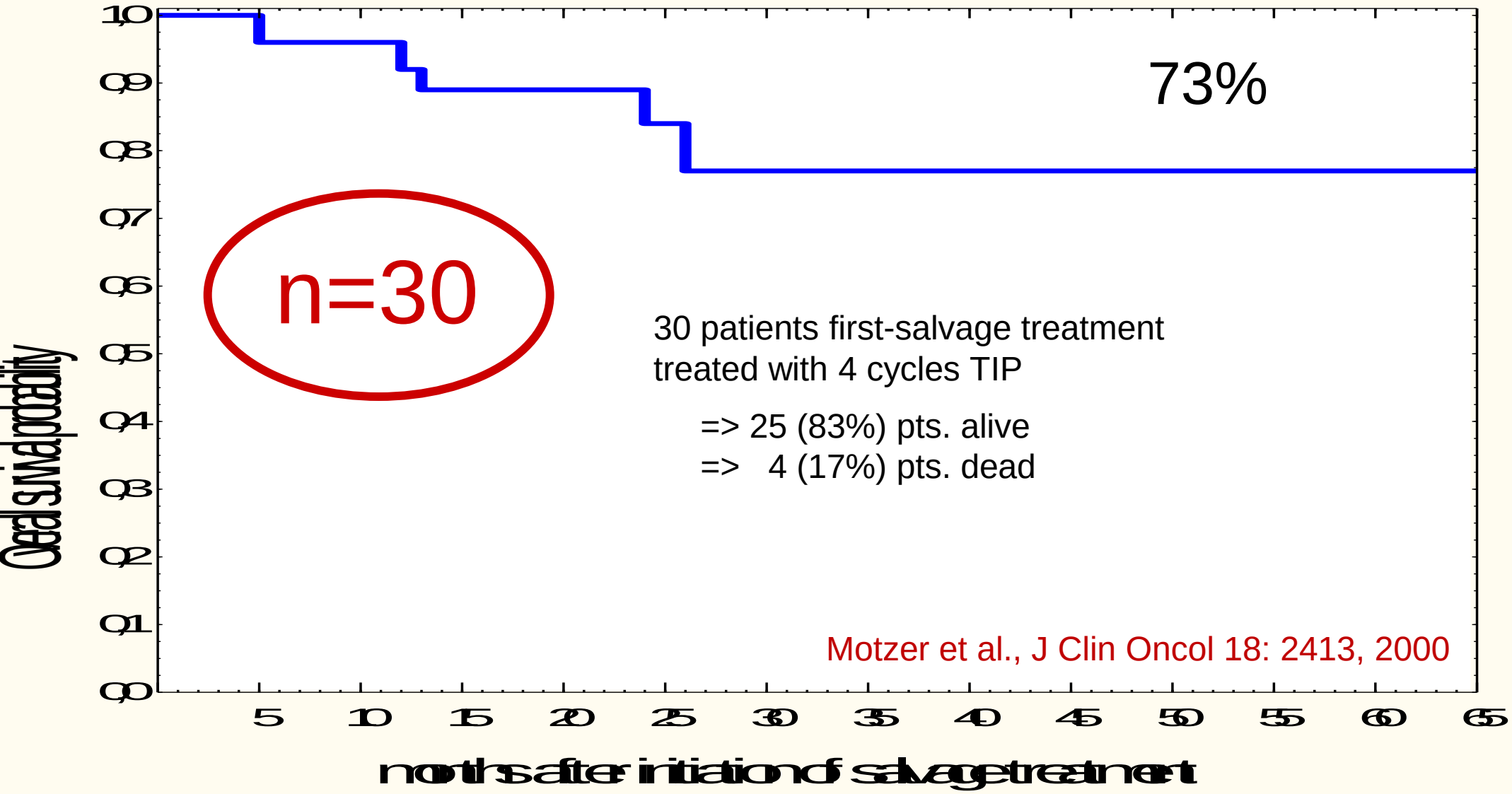
What treatment would you recommend ?

- 26 year old male, gonadal primary, 80% EC, 20% Seminoma
- "good prognosis disease" with low volume abdominal metastases treated with 3x BEP => CR
- follow-up after 3 months AFP from normal to 524 ng/ml
- abdominal lymphnodes 3 cm, new pulmonary lesion 1 cm

Raise your hands and give me your vote !

- green = 4x conventional-dose salvage treatment e.g. with VeIP, VIP or TIP
- red = PBPC mobilizing chemo followed by 3x high-dose salvage treatment
- yellow = I haven't got a clue; would phone up Joerg Beyer and ask him

Survival after conventional-dose first-salvage treatment



Challenge of TIP data

- very small, single center, phase II trial
- highly positively selected patient population
- 50% did not receive modern type first-line treatment
- mixed bag of seminoma and non-seminoma
- some mature teratoma probably cured by surgery
- treated 1994-1998, no long-term follow-up

Paclitaxel, Ifosfamide, and Cisplatin Second-Line Therapy for Patients With Relapsed Testicular Germ Cell Cancer

All favorable prognostic factors for achieving a complete response to cisplatin plus ifosfamide conventional-dose salvage therapy had to be met and were as follows: (1) gonadal primary tumor site; (2) prior treatment limited to one program or six or fewer prior cycles of cisplatin; and (3) either a complete response or a partial response with normal serum tumor markers to first-line chemotherapy program.

Histology		
Nonseminoma	27	90
Seminoma	3	10
Prior chemotherapy regimen		
Etoposide plus cisplatin	15	50
Bleomycin, etoposide, cisplatin	10	33
VAB-6 ± others	3	10
Etoposide plus carboplatin	2	7

Journal of Clinical Oncology, Vol 18, No 12 (June), 2000: pp 2413-2418

Combination of Paclitaxel, Ifosfamide, and Cisplatin Is an Effective Second-Line Therapy for Patients With Relapsed Testicular Germ Cell Tumors

G. Varuni Kondagunta, Jennifer Bacik, Alessia Donadio, Dean Bajorin, Stephanie Marion, Joel Sheinfeld, George J. Bosl, and Robert J. Motzer

Treatment consisted of four cycles of TIP administered 21 days apart. The first 30 patients were treated with a 6-day regimen as previously described.[15]

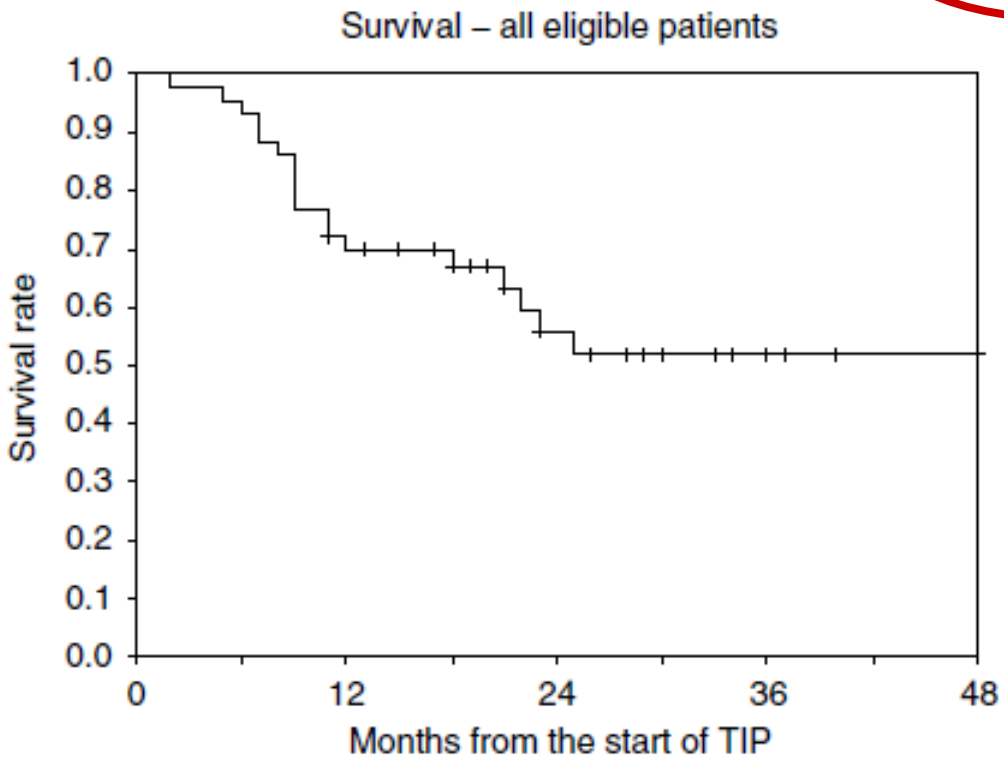
Histology		
Nonseminoma	41	89
Seminoma	5	11
Prior chemotherapy regimen		
Etoposide + cisplatin ± bleomycin	34	74
VAB-6 or other vinblastine-based therapy*	9	19
Etoposide + carboplatin ± bleomycin	3	7

J Clin Oncol 23:6549-6555. © 2005

A phase II trial of TIP (paclitaxel, ifosfamide and cisplatin) given as second-line (post-BEP) salvage chemotherapy for patients with metastatic germ cell cancer: a medical research council trial

British Journal of Cancer (2005) **93**(2), 178–184

n=43



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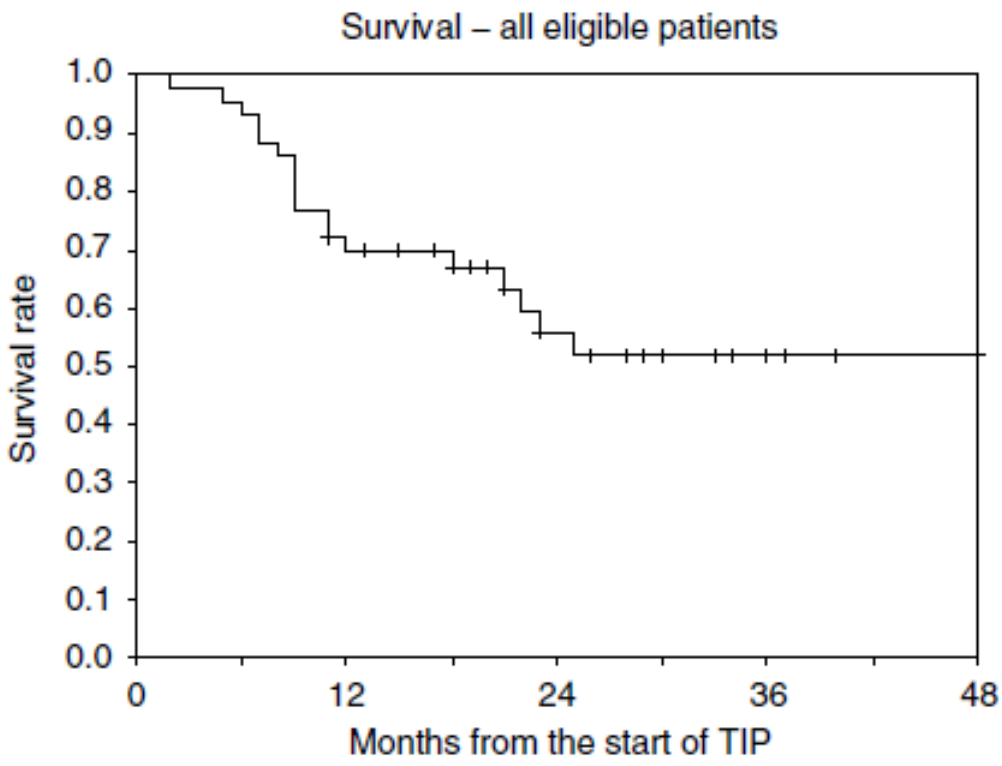

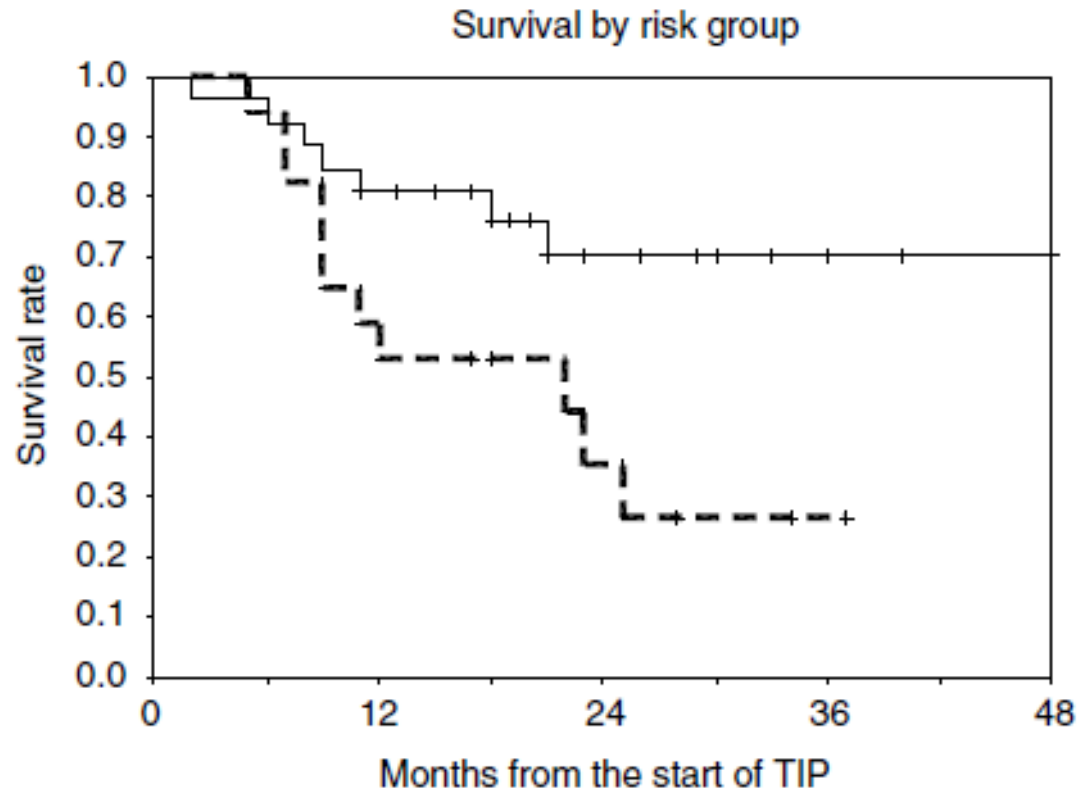

A phase II trial of TIP (paclitaxel, ifosfamide and cisplatin) given as second-line (post-BEP) salvage chemotherapy for patients with metastatic germ cell cancer: a medical research council trial

Eligibility

Male patients with the following characteristics were eligible: (i) first relapse after previous BEP chemotherapy given for metastatic GCC, (ii) either sequentially rising serum markers (AFP and/or HCG) or biopsy-proven and unresectable GCC; (iii) age 16–65 years; (iv) ECOG performance status 0–2; (v) glomerular filtration rate of $\geqslant 50\,\mathrm{ml\,h^{-1}}$ and (vi) no evidence of brain metastases.

Histology		
Seminoma	9	20.90
Nonseminoma	33	76.70
Not known (high HCG, no biopsy)	1	2.30
Relapse interval		
<2 months	4	9.30
2 months to 2 years	30	69.80
>2 years	9	20.90

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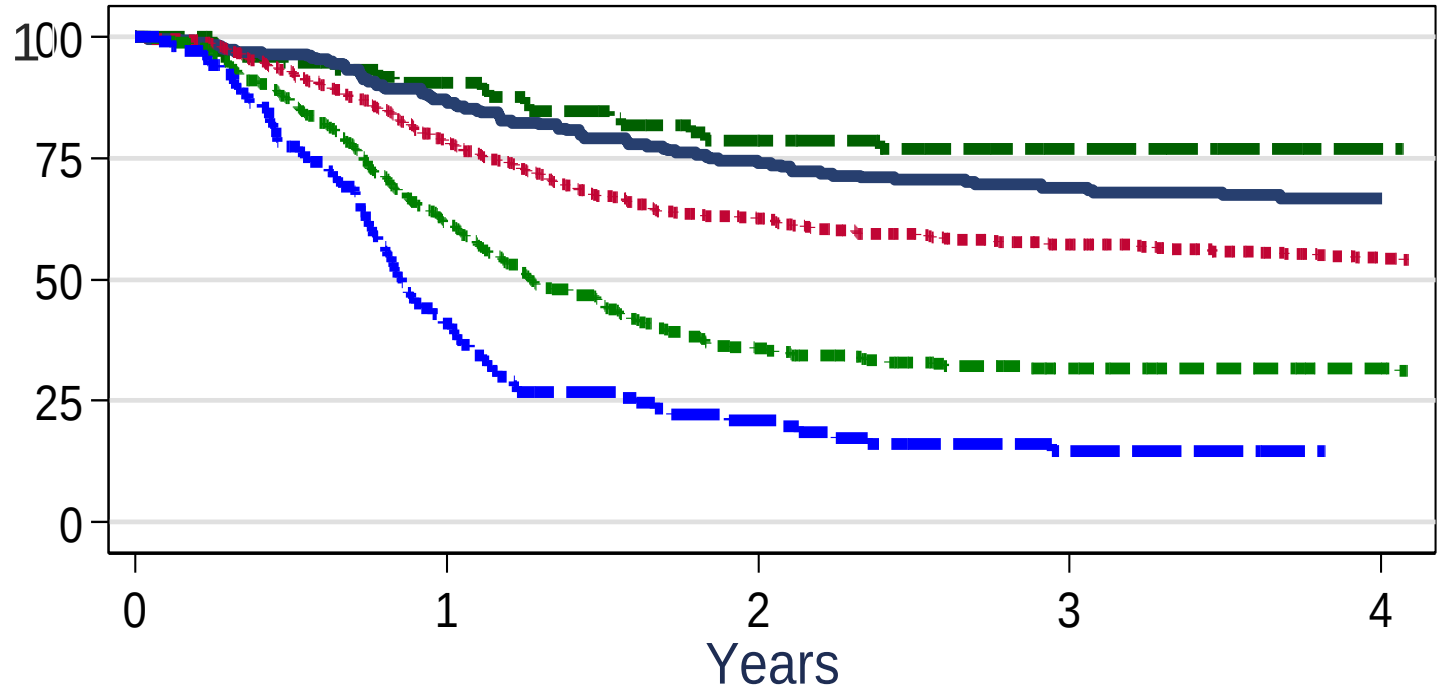
JOURNAL OF CLINICAL ONCOLOGY
VOLUME 28 · NUMBER 33 · NOVEMBER 20 2010

n=1594

Overall Survival

All patients



Number at risk					
Very Low	76	64	50	40	35
Low	257	214	172	135	107
Intermediate	646	475	351	276	219
High	351	203	109	74	61
Very High	105	38	18	10	0

VOLUME 28 · NUMBER 33 · NOVEMBER 20 2010

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ORIGINAL REPORT

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	—	—	

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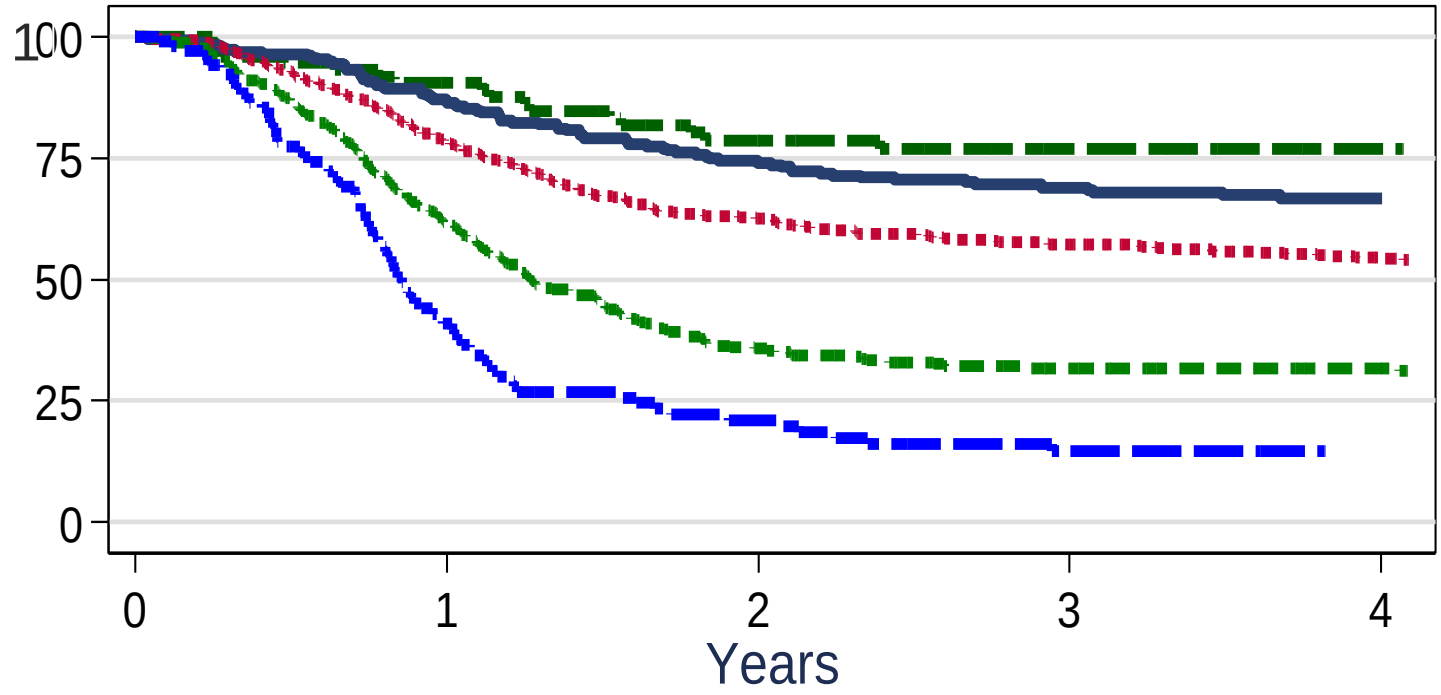

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Original article

Annals of Oncology 16: 1152–1159, 2005
doi:10.1093/annonc/mdi228
Published online 31 May 2005

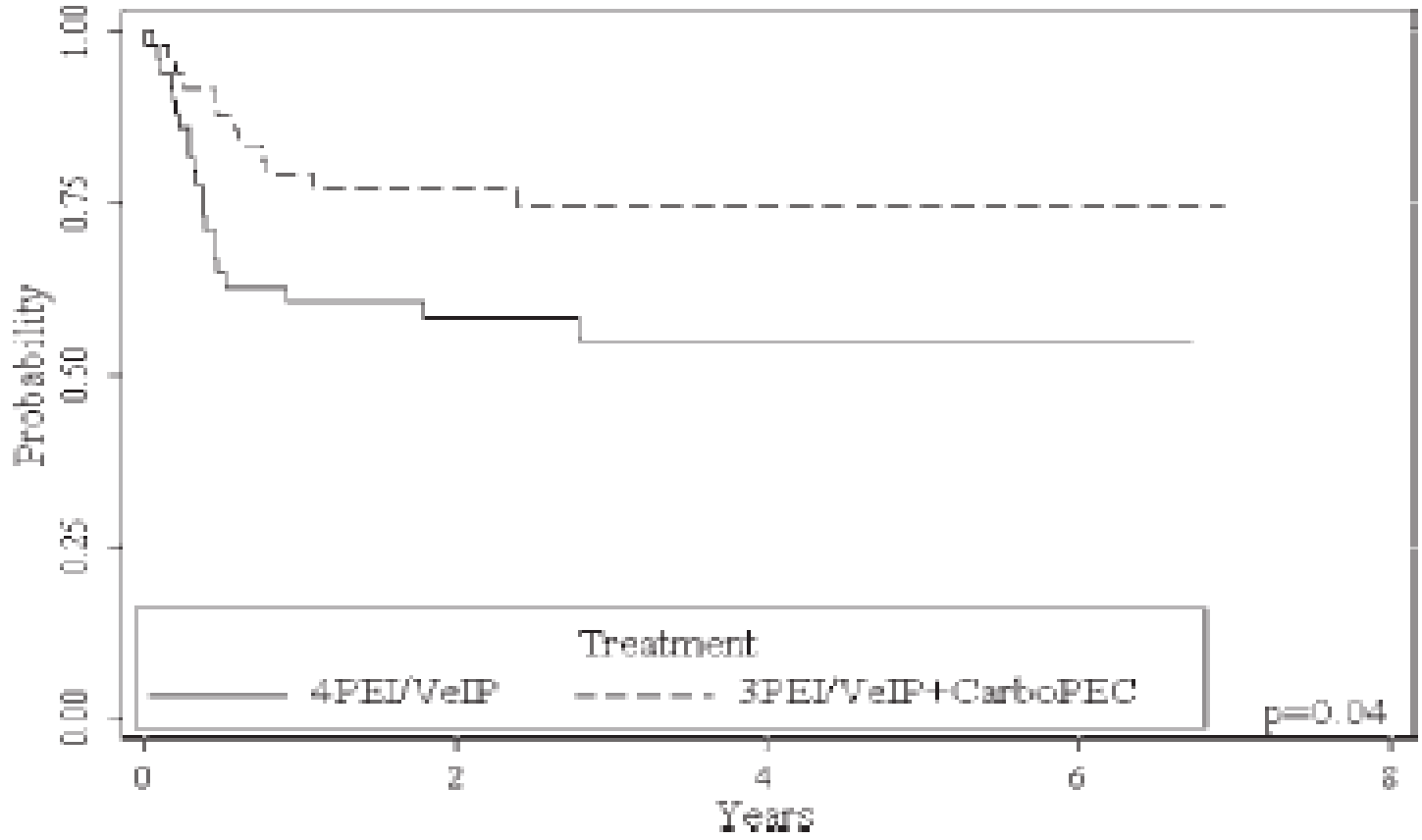
A randomised trial of high-dose chemotherapy in the salvage treatment of patients failing first-line platinum chemotherapy for advanced germ cell tumours

J.-L. Pico[1], G. Rosti[2], A. Kramar[3]*, H. Wandt[4], V. Koza[5], R. Salvioni[6], C. Theodore[1], G. Lelli[7], W. Siegert[8], A. Horwich[9], M. Marangolo[2], W. Linkesch[10], G. Pizzocaro[6], H.-J. Schmoll[11], J. Bouzy[1], J.-P. Droz[12] & P. Biron[12], for the Genito-Urinary Group of the French Federation of Cancer Centers (GETUG-FNCLCC), France and the European Group for Blood and Marrow Transplantation (EBMT)

[1]Institut Gustave Roussy, Villejuif, France; [2]Ospedale Santa Maria Delle Croci, Ravenna, Italy; [3]CRLC Val d'Aurelle, Montpellier, France; [4]Klinikum Nord U. Inst. F. Onkologie, Nuremberg, Germany; [5]Charles University Hospital, Pilsen, Czech Republic; [6]Istituto Nazionale Tumori, Milan, Italy; [7]Casa Sollievo della Sofferenza, S. Giovanni Rotondo, Italy; [8]Universitatklinikum Rudolf Virchow, Berlin, Germany; [9]The Royal Marsden Hospital, London, UK; [10]Medizinische Universitatklinik, Graz, Austria; [11]Martin Luther Universität, Halle, Germany; [12]CAC Léon Bérard, Lyon, France

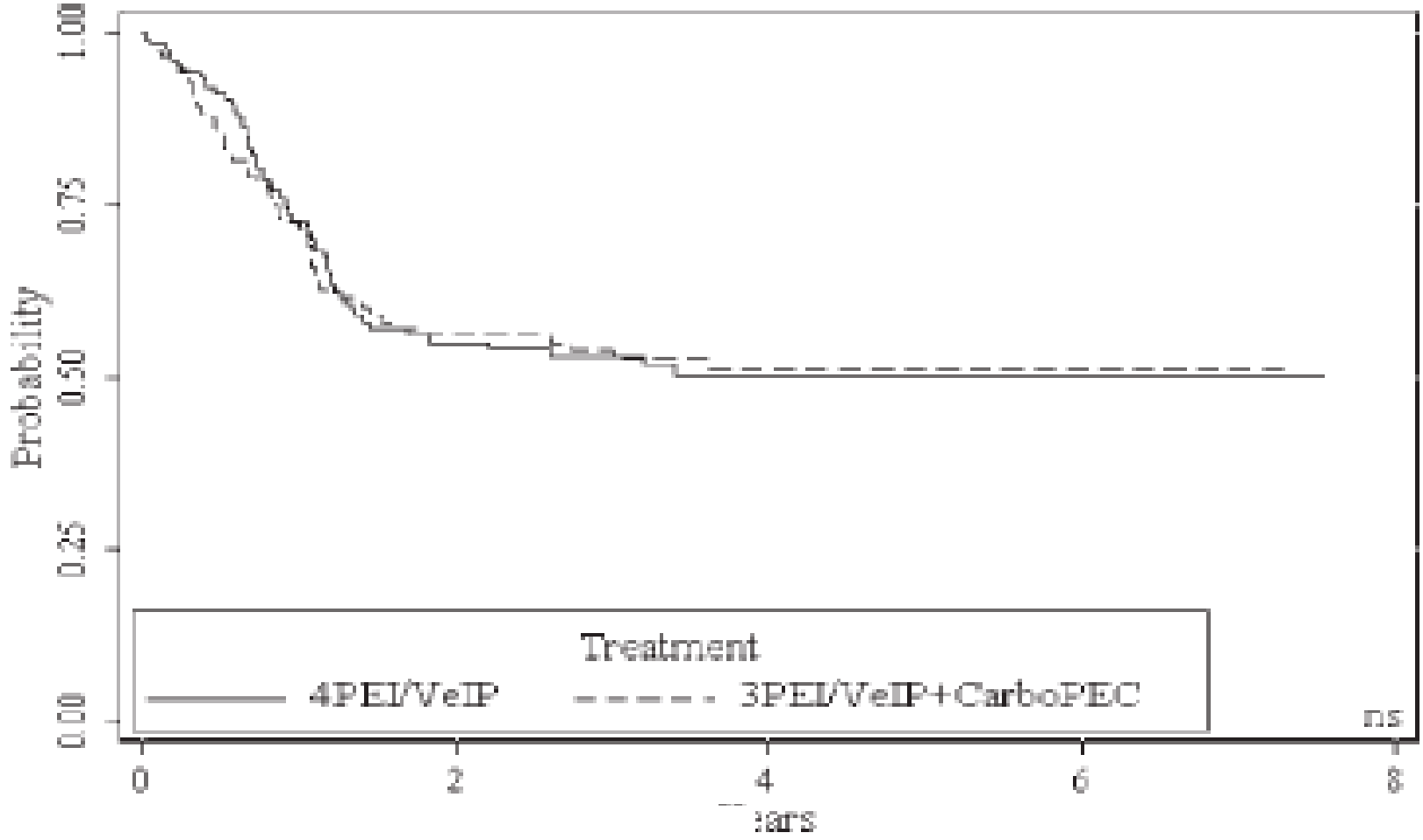
Received 2 December 2004; revised 21 March 2005; accepted 30 March 2005

A randomised trial of high-dose chemotherapy in the salvage treatment of patients failing first-line platinum chemotherapy for advanced germ cell tumours



Pico et al 2005

A randomised trial of high-dose chemotherapy in the salvage treatment of patients failing first-line platinum chemotherapy for advanced germ cell tumours



Pico et al 2005

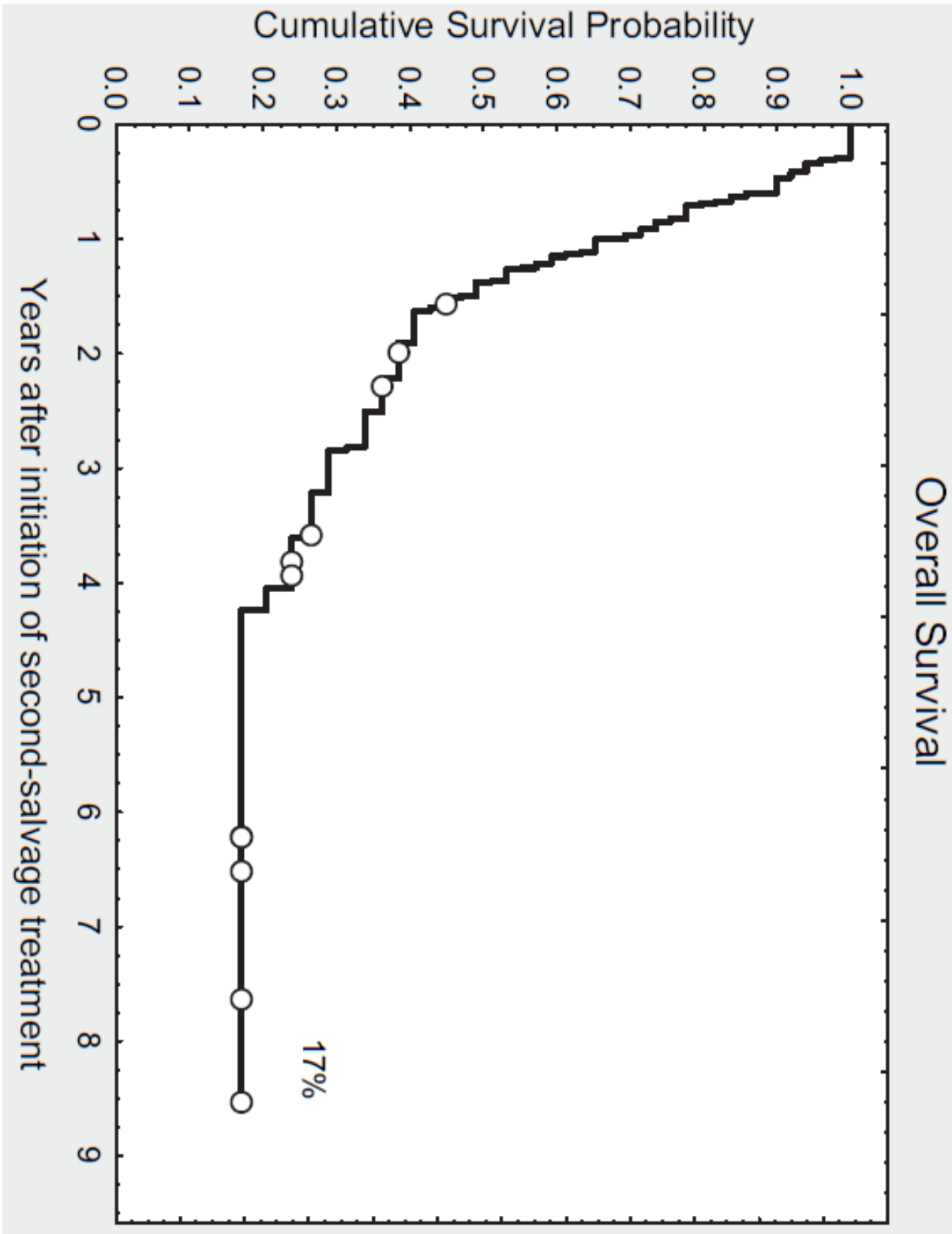
Summary conventional-dose salvge

- Two phase II trials favor conventional-dose salvage chemo in "good risk" patients e.g. paclitaxel, cisplatin, ifosfamide
- One randomized trial failed to show superiority of high-dose dose over conventional-dose chemotherapy
- High-dose chemo might still be curative in second or even subsequent salvage treatment

Annals of Oncology 21: 820–825, 2010
doi:10.1093/annonc/mdp366
Published online 11 October 2009

High-dose chemotherapy (HDCT) as second-salvage treatment in patients with multiple relapsed or refractory germ-cell tumors

A. Lorch[1], A. Neubauer[1], M. Hackenthal[2], A. Dieing[3], J. T. Hartmann[4], O. Rick[5], C. Bokemeyer[6] & J. Beyer[2*]



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n=1594

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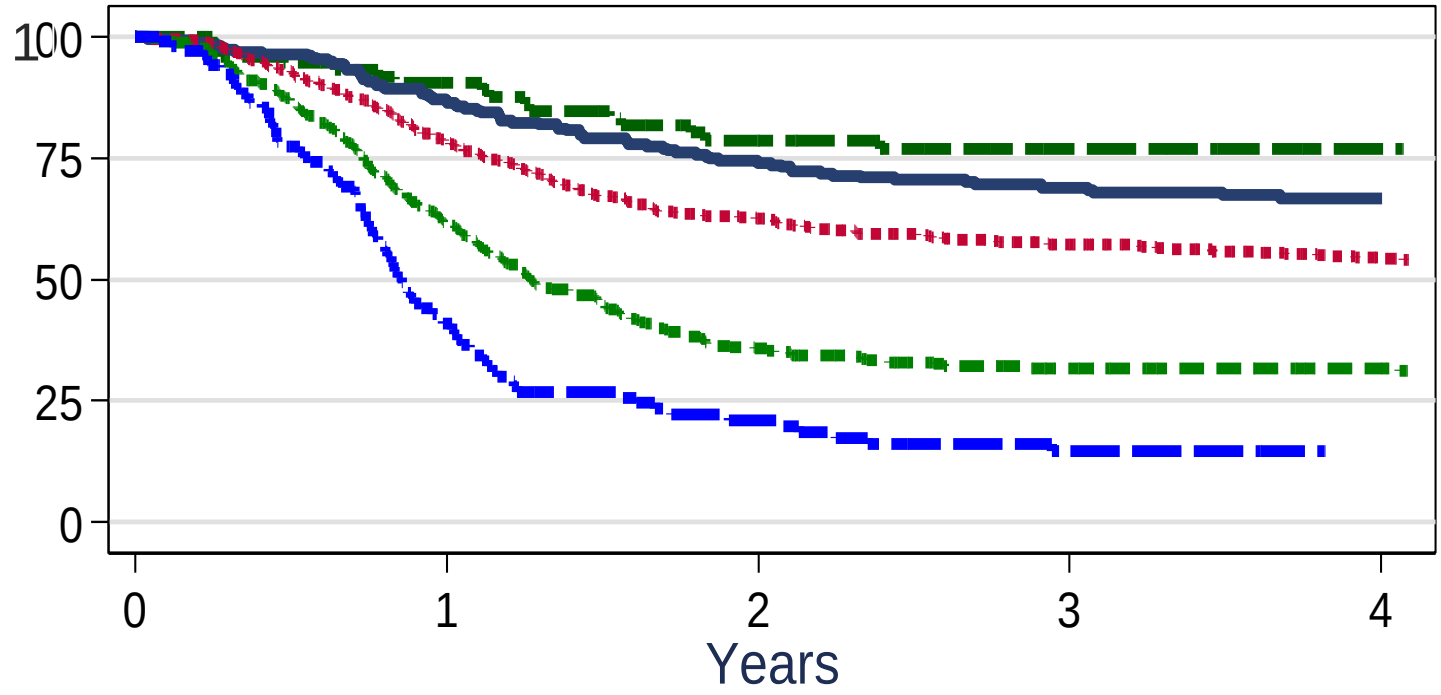
All patients



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Does high-dose chemotherapy make a difference?

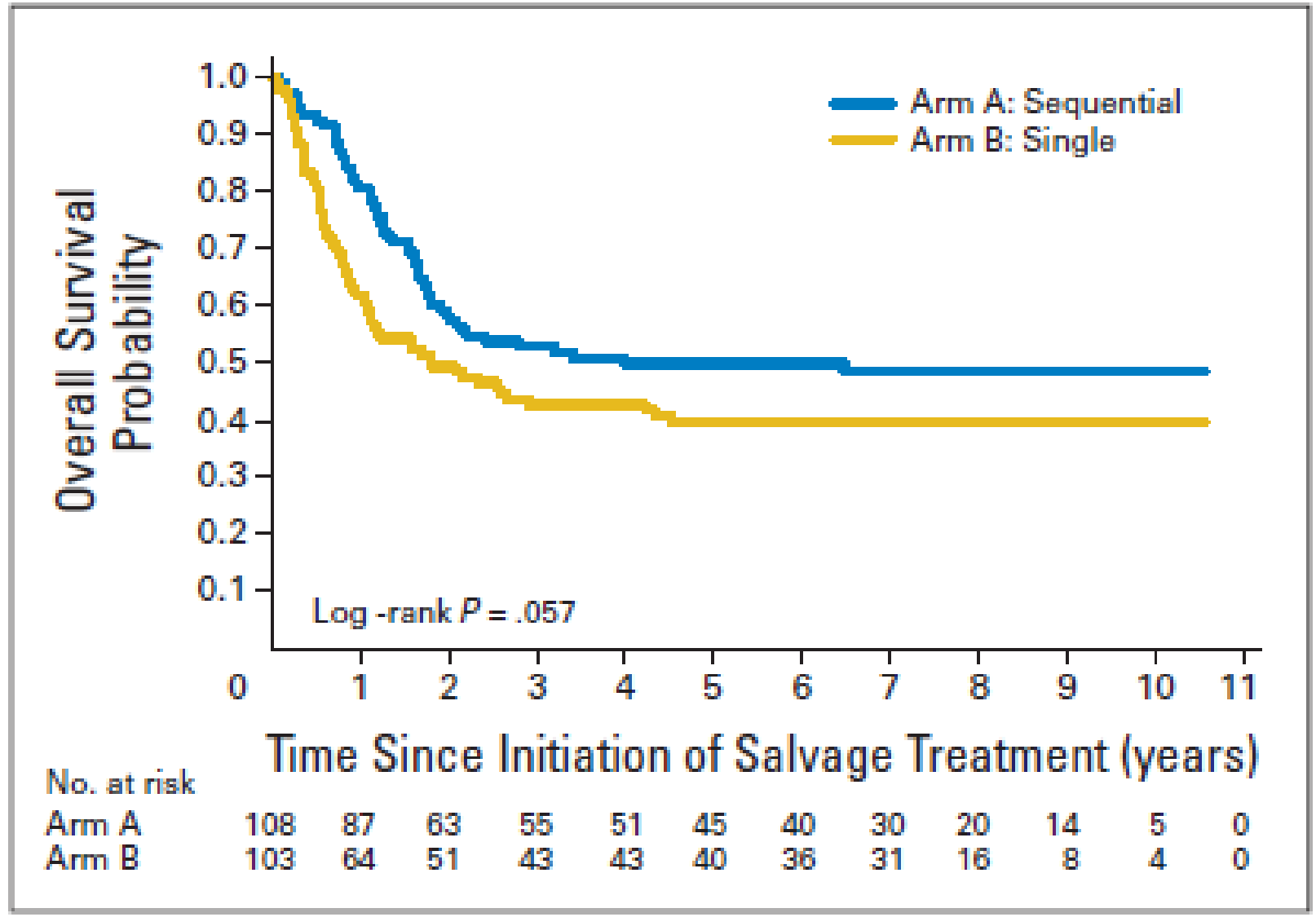
Yes, it does !

High-dose salvage

First author	Year published	Regimen used	Patients included	Treatment Period
Nichols	1991	Carbo, Eto	38	1988 - 1989
Bhatia	2000		65	1992 - 1998
Motzer	2000		37	1994 - 1997
De Giorgi	2005		59	1987 - 1999
Einhorn	2007		184	1996 - 2004
Kondagunta	2007		48	1998 - 2003
Lorch	2007		108	1999 - 2004
Siegert	1994	Carbo, Eto, Ifo	74	1989 - 1992
Lotz	1995		31	
Margolin	1996		20	1989 - 1995
Pico	2007	Carbo, Eto, Cyclo	135	1994 - 2001
Lorch	2007		103	1999 - 2004
Rodenhuis	1999	Carbo, Eto, Thio	35	1994 - 1997
Rick	2001	+/- Cyclo or Ifo	80	1995 - 1997
Lotz	2005		45	1998 - 2001

JOURNAL OF CLINICAL ONCOLOGY

Sequential Versus Single High-Dose Chemotherapy in Patients With Relapsed or Refractory Germ Cell Tumors: Long-Term Results of a Prospective Randomized Trial



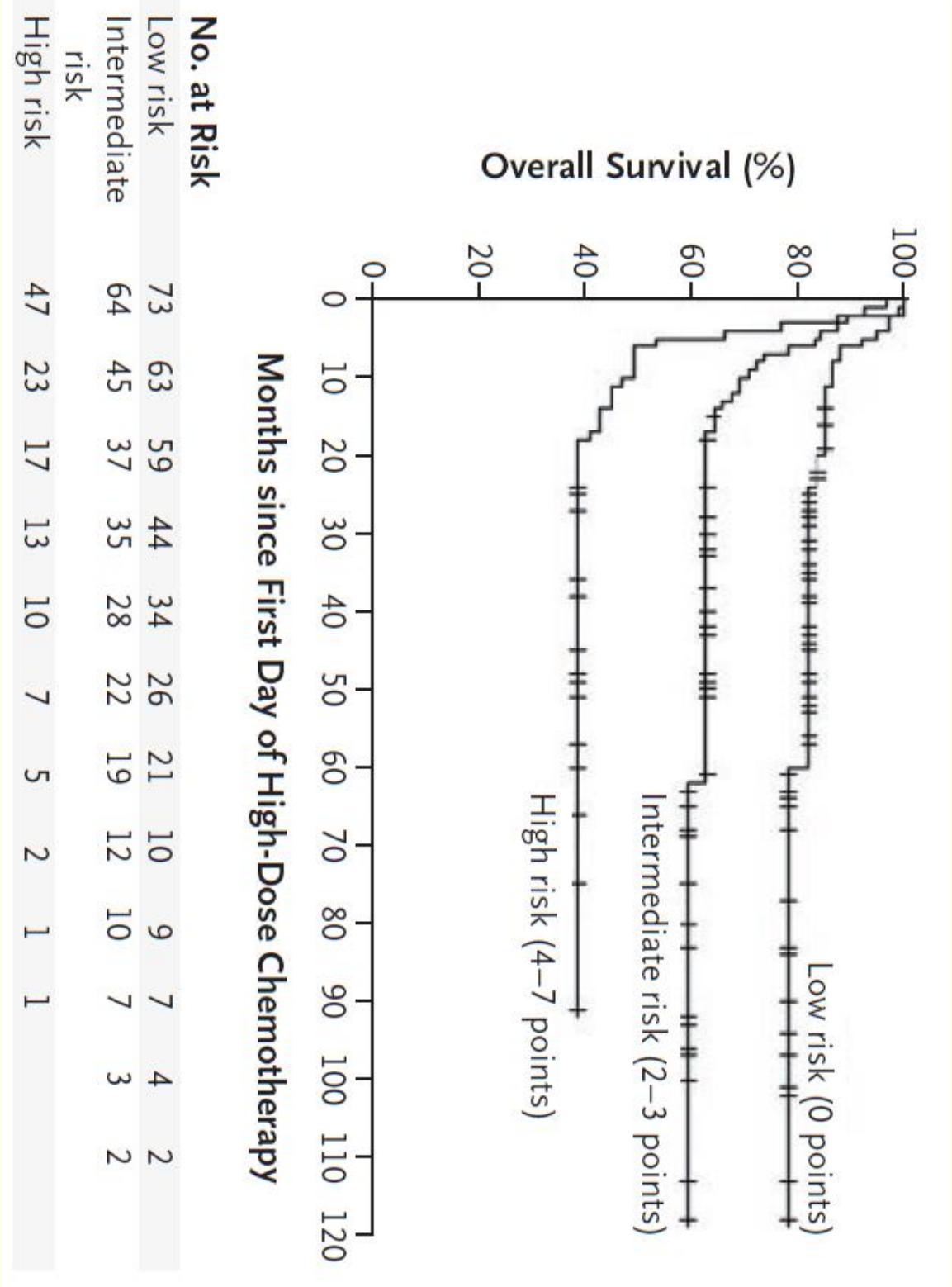
Survival rates according to prognostic categories

Prognostic category	N	(%)	PFS at 2-years	95% CI	OS at 3-years	95% CI
First salvage: very low-risk	17	(8%)	82%	55% - 94%	82%	55% - 94%
Arm A	8	(4%)	63%	24% - 86%	63%	23% - 86%
Arm B	9	(4%)	100%	-	100%	-
First salvage: low-risk	32	(15%)	64%	44% - 79%	59%	40% - 74%
Arm A	18	(9%)	69%	40% - 86%	61%	35% - 79%
Arm B	14	(7%)	58%	27% - 80%	56%	26% - 77%
First salvage: intermediate risk	79	(38%)	52%	40% - 63%	52%	40% - 62%
Arm A	42	(20%)	51%	35% - 65%	55%	39% - 68%
Arm B	37	(18%)	54%	36% - 69%	49%	32% - 63%
First salvage: high-risk	37	(18%)	34%	19% - 50%	32%	18% - 47%
Arm A	18	(9%)	50%	26% - 70%	56%	31% - 75%
Arm B	19	(9%)	14%	2% - 37%	11%	2% - 28%
First salvage: very high-risk	7	(3%)	none	-	none	-
Second or subsequent salvage	30	(14%)	24%	11% - 41%	30%	15% - 47%
Arm A	15	(7%)	33%	12% - 56%	40%	17% - 63%
Arm B	15	(7%)	15%	2% - 38%	20%	5% - 42%
No unequivocal classification	9	(4%)	76%	33% - 94%	67%	28% - 88%

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.

N Engl J Med 2007;357:340-8.



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

n = 1594 Patients included in prognostic factor analysis

n = 773 treated with CDCT	**n = 821 treated with HDCT**
n = 37 very low risk	n = 39 very low risk
n = 122 low risk	n = 135 low risk
n = 318 intermediate risk	n = 328 intermediate risk
n = 152 high risk	n = 199 high risk
n = 54 very high risk	n = 51 very high risk

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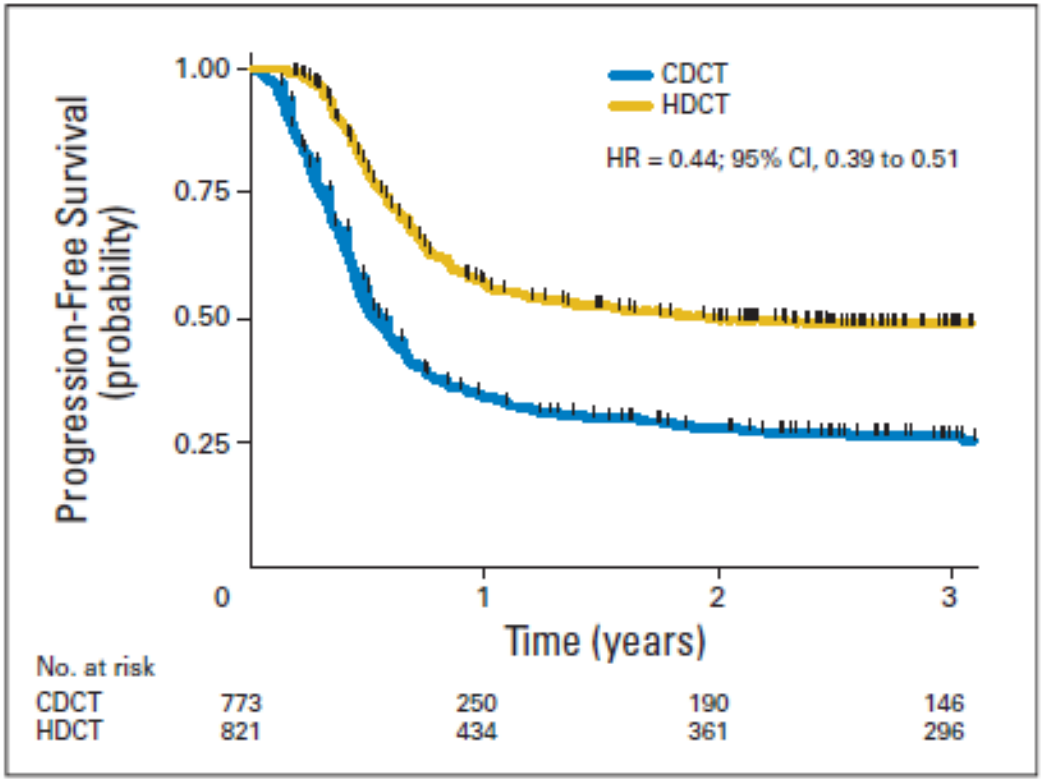

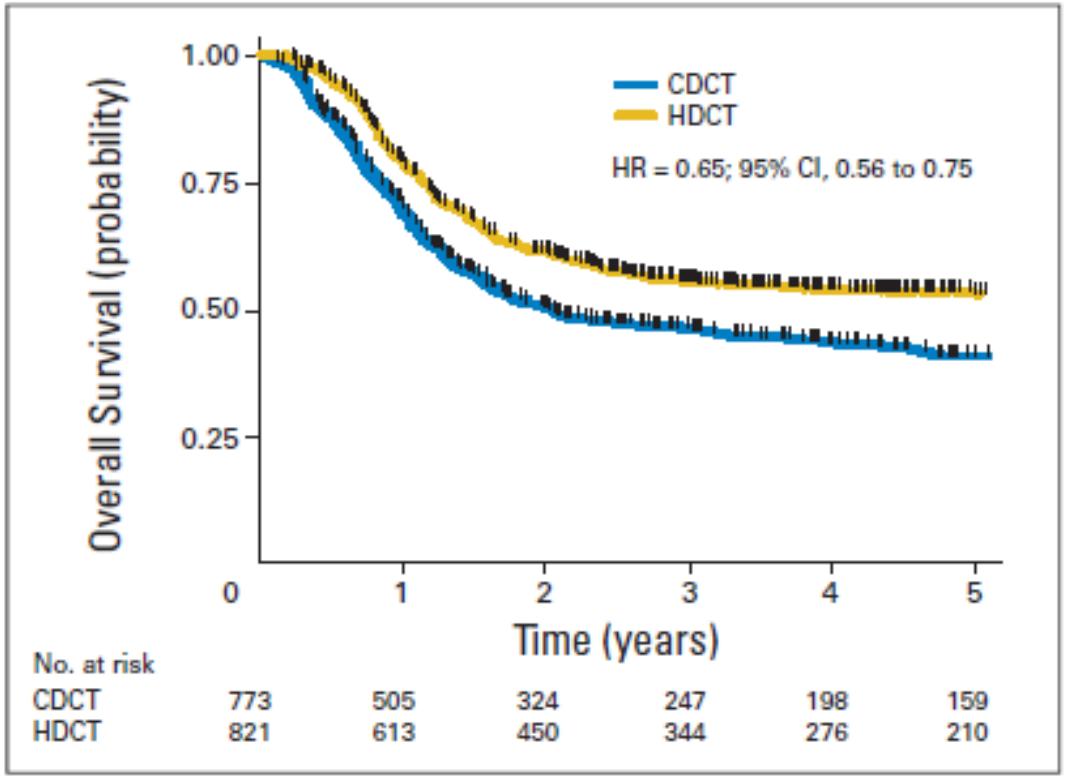

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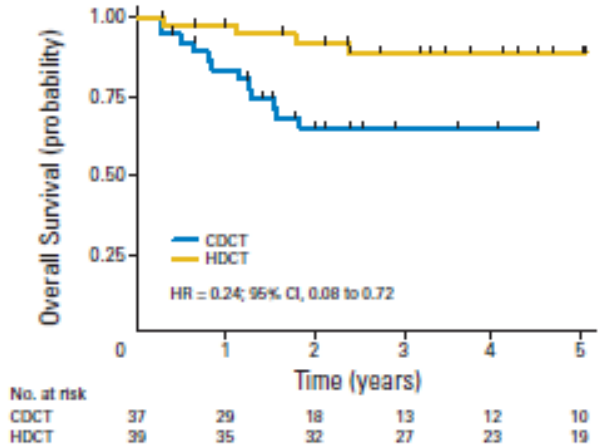
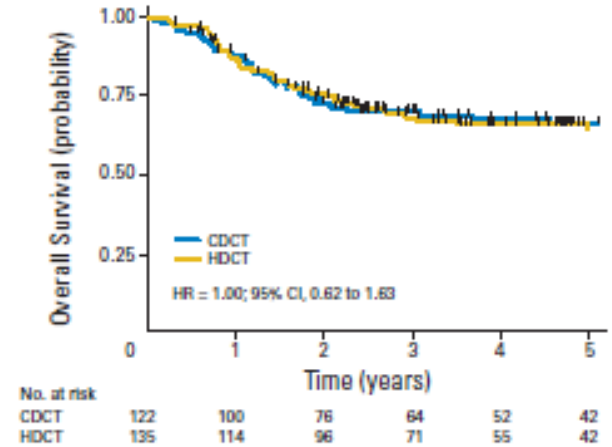
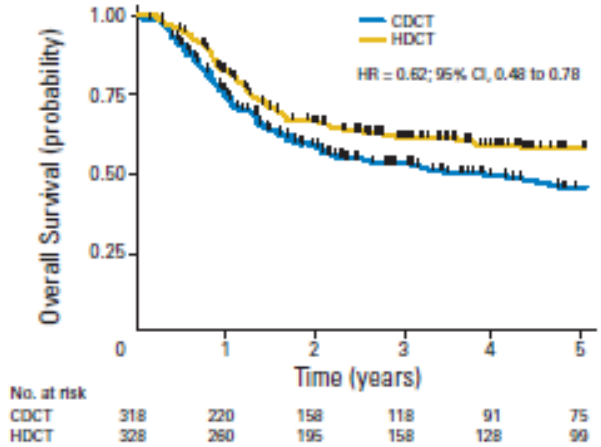
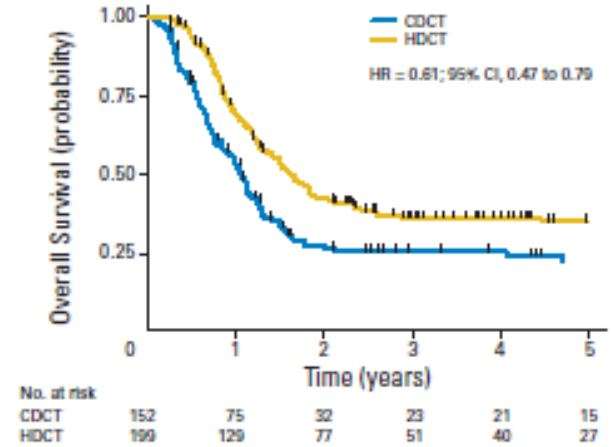
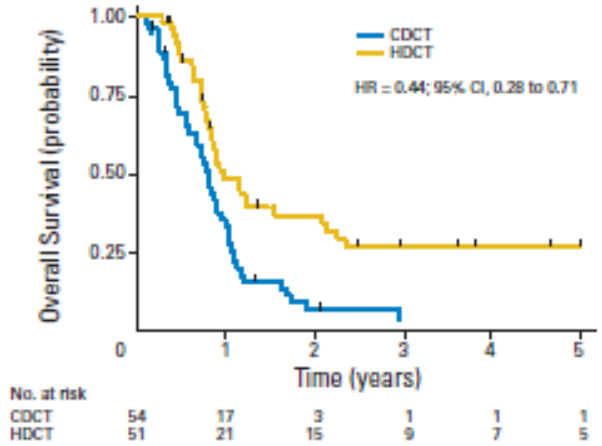




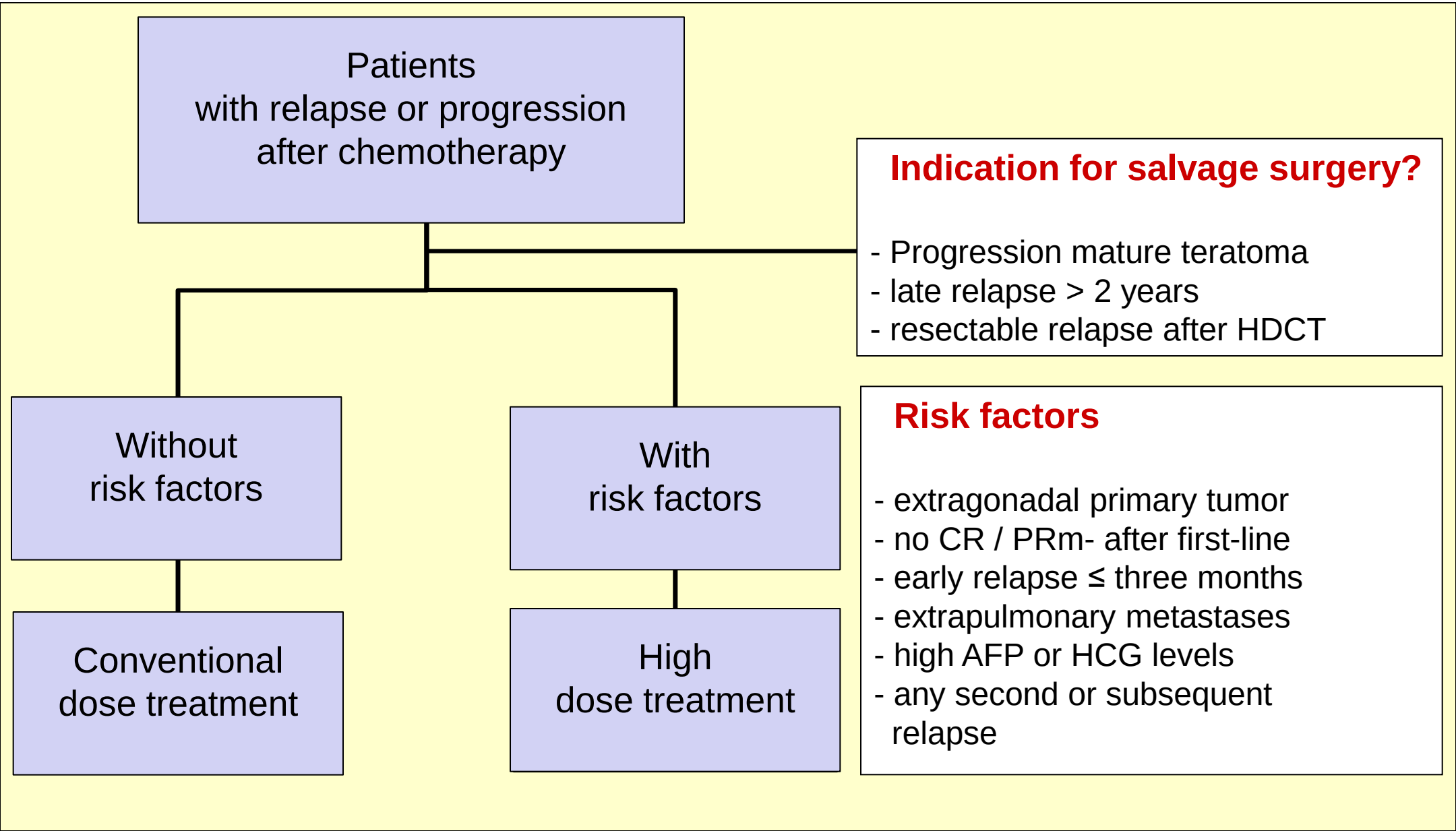






Overall survival according to risk categories

One possible strategy for first-salvage



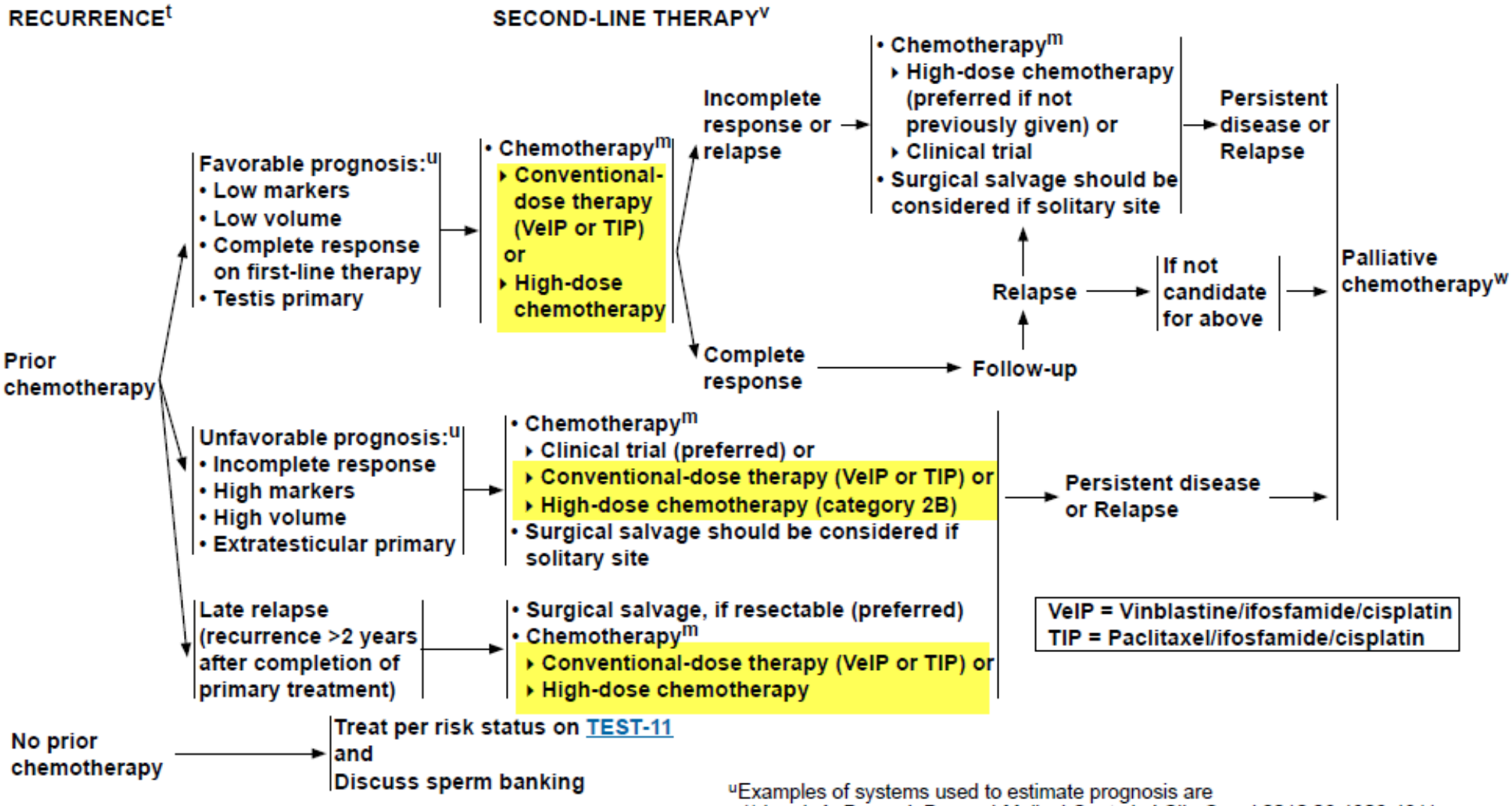
Guidelines on Testicular Cancer

P. Albers (chair), W. Albrecht, F. Algaba,
C. Bokemeyer, G. Cohn-Cedermark, K. Fizazi,
A. Horwich, M.P. Laguna, N. Nicolai, J. Oldenburg

High dose chemotherapy offered no advantage as first salvage treatment according to the results of the randomised IT 94 trial in good prognosis patients (256). Patients with good prognostic features should therefore be offered conventional-dose first salvage treatment. However, several phase II trials, as well as one retrospectively matched-pair analysis, have shown an improvement in survival in poor-prognosis patients with early intensification of first-salvage treatment using high-dose chemotherapy (257,262,273,274). All of these patients should, if possible, be entered into ongoing studies to define the optimal approach to salvage treatment, and should be referred to centres experienced in caring for relapse and/or refractory patients (275,276).

NCCN Guidelines Version 1.2014
Testicular Cancer - Nonseminoma

NCCN Guidelines Index
Testicular Cancer TOC
Discussion



[m] See Second Line Chemotherapy Regimens for Germ Cell Tumors (TEST-D).

[t] It is preferred that patients with recurrent nonseminoma be treated at centers with expertise in the management of this disease.

[u] Examples of systems used to estimate prognosis are
1) Lorch A, Beyer J, Bascoul-Mollevi C, et al. J Clin Oncol 2010;28:4906-4911.
2) Einhorn LH, Williams SD, Chamness A, et al. New Engl J Med 2007;357:340-348.
3) Motzer RJ, Geller NL, Tan CC, et al. Cancer 1991;67:1305-1310.

[v] Includes best supportive care.

[w] See Subsequent Chemotherapy Regimens for Metastatic Germ Cell Tumors (TEST-E).

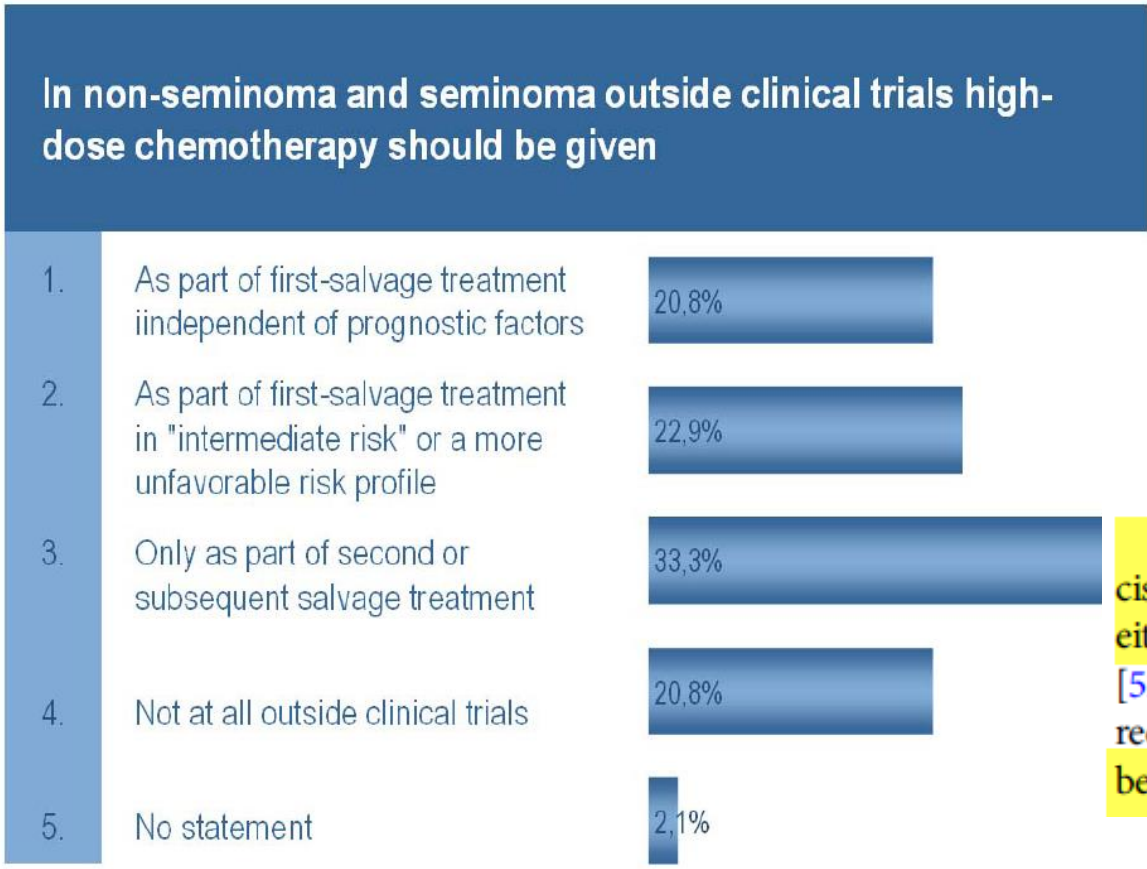
Annals of Oncology 24 (Supplement 6): vi125–vi132, 2013
doi:10.1093/annonc/mdt304

Testicular seminoma and non-seminoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

Conclusive recommendations as to an optimal salvage approach in patients relapsing after cisplatin-based first-line treatment cannot be made at present.

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



Seminoma and non-seminoma patients who relapse after full cisplatin-based first-line chemotherapy can be treated using either conventional-dose chemotherapy (CDCT) or HDCT [52–57]. Their prognosis should be assessed using the most recent international prognostic score [54]. No consensus could be reached in respect to their optimal first-salvage management

What treatment would you recommend ?

- 26 year old male, gonadal primary, 80% EC, 20% Seminoma
- "good prognosis disease" with low volume abdominal metastases treated with 3x BEP => CR
- follow-up after 3 months AFP from normal to 524 ng/ml
- abdominal lymphnodes 3 cm, new pulmonary lesion 1 cm

Raise your hands and give me your vote !

- green = 4x conventional-dose salvage treatment e.g. with VeIP, VIP or TIP
- red = PBPC mobilizing chemo followed by 3x high-dose salvage treatment
- yellow = I haven't got a clue; would phone up Joerg Beyer and ask him

Further course

- 26 year old male, gonadal primary, 80% EC, 20% Seminoma
- "good prognosis disease" with low volume abdominal metastases treated with 3x BEP => CR
- follow-up after 3 months AFP from normal to 524 ng/ml
- abdominal lymphnodes 3 cm, new pulmonary lesion 1 cm
- Two cycles of TIP with PRm+, but clear-cut AFP progression prior to the third cycle

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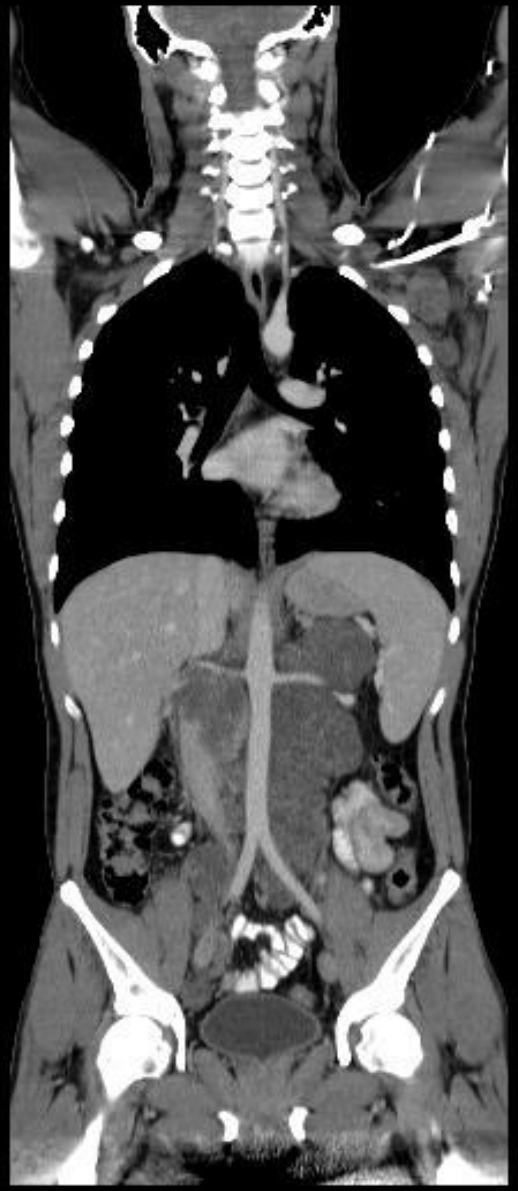
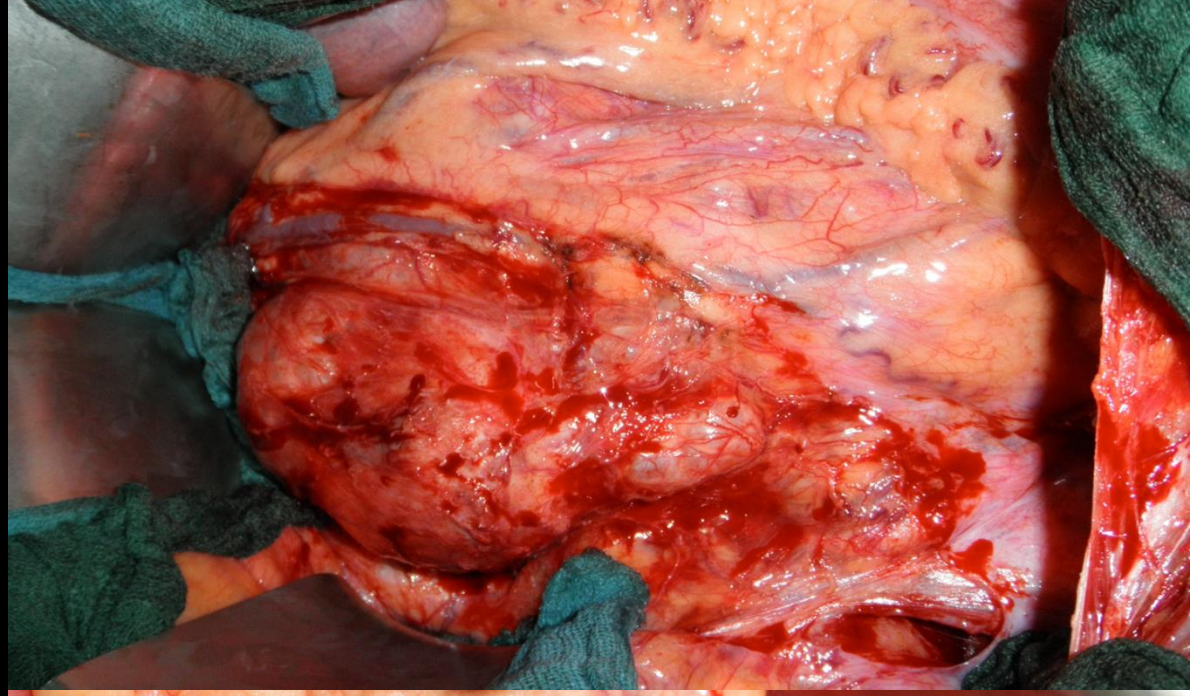
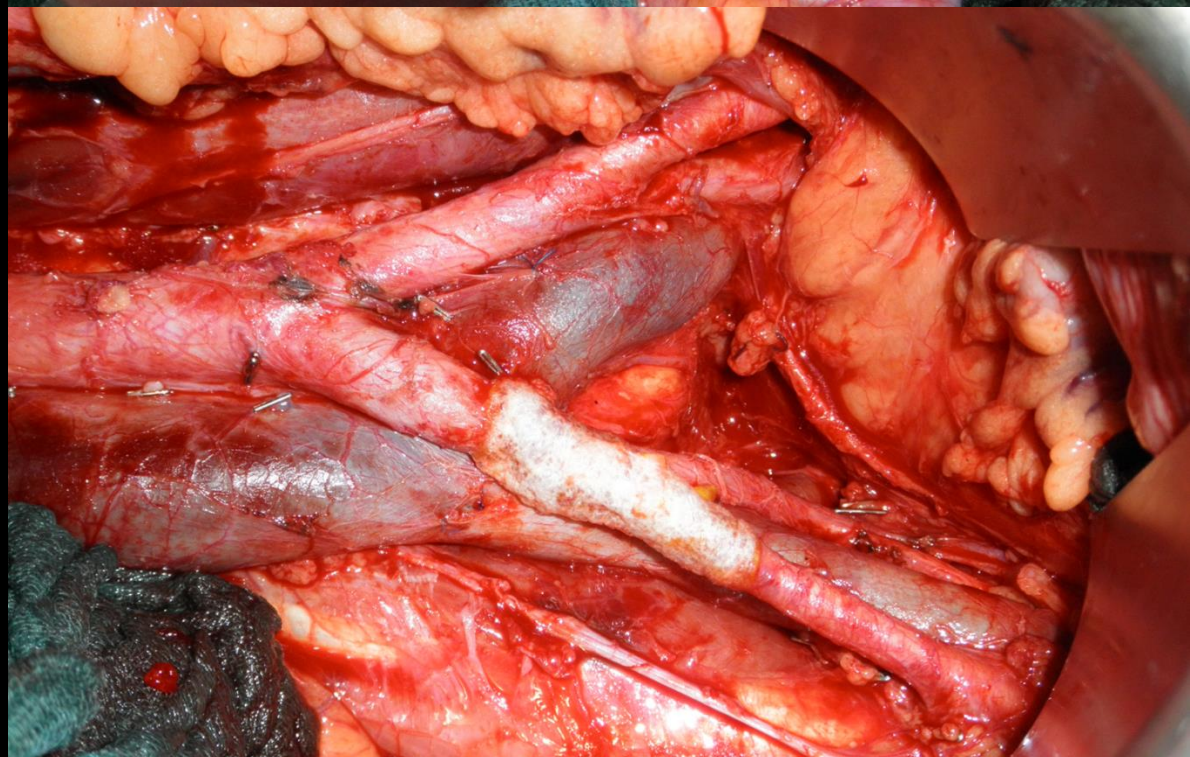
- Successful mobilization of PBPC with high-dose etoposide plus G-CSF
- HDCT => PRm- followed by abdominal surgery => $CR_{Nekrosis}$

High dose chemotherapy plus PBPC regimens

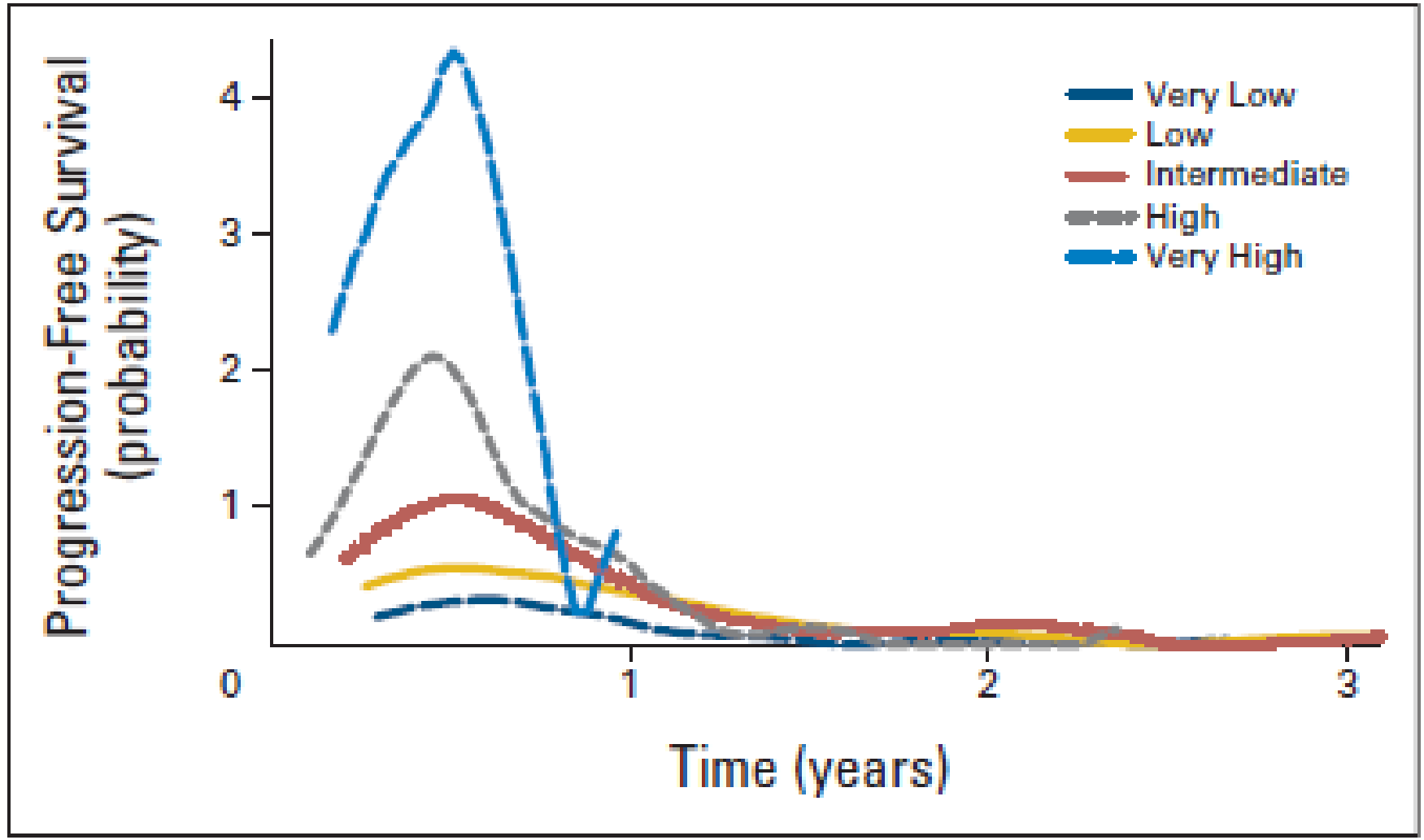
Lorch JCO 2012	**Sequential**	**Three cycles**
Carbo	500 mg/m^2	Day 1-3
Eto	500 mg/m^2	Day 1-3
Motzer JCO 2000	**Sequential**	**Three cycles**
Carbo	AUC 8	Day 1-3
Eto	400 mg/m^2	Day 1-3
Einhorn NEJM 2011	**Sequential**	**Two cycles**
Carbo	750 mg/m^2	Day 1-3
Eto	750 mg/m^2	Day 1-3







Progression after Salvage Treatment



J Clin Oncol 28:4906-4911. © 2010

Patient No 2

- 48 years old, right-sided non-seminoma
  (40% chorio, 30% embryonal, 10% yolk-sac, 10% seminoma, 10% teratoma)
- Increased abdominal lymphnodes, few pulmonary metastases
- Markers: HCG 37.401 U/l, AFP 499 ng/ml, LDH 432 U/l

Patient No 2

- 48 years old, right-sided non-seminoma
  (40% chorio, 30% embryonal, 10% yolk-sac, 10% seminoma, 10% teratoma)
- Increased abdominal lymphnodes, few pulmonary metastases
- Markers: HCG 37.401 U/l, AFP 432 ng/ml, LDH 432 U/l pre OP
  Markers: HCG 2.927 U/l, AFP 60 ng/ml, LDH 377 U/l post OP

Patient No 2

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- Markers: HCG 37.401 U/l, AFP 432 ng/ml, LDH 432 U/l pre OP
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- Treatment with BEP x 3, CR with chemo alone

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- Treatment with BEP x 3, CR with chemo alone, 3 months check o.k.
- Check at 6 months symptomatic with SOB.
  => Lung, liver, spleen, kidney, multiple brain metastases
  => HCG 4.606 U/l, AFP 3.1 ng/ml, LDH 702 U/l

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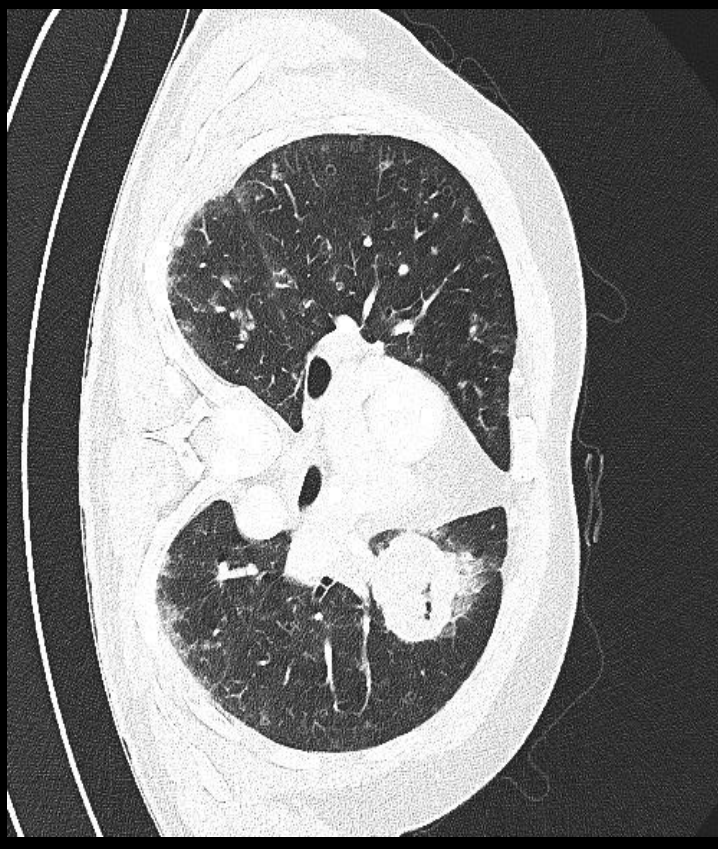
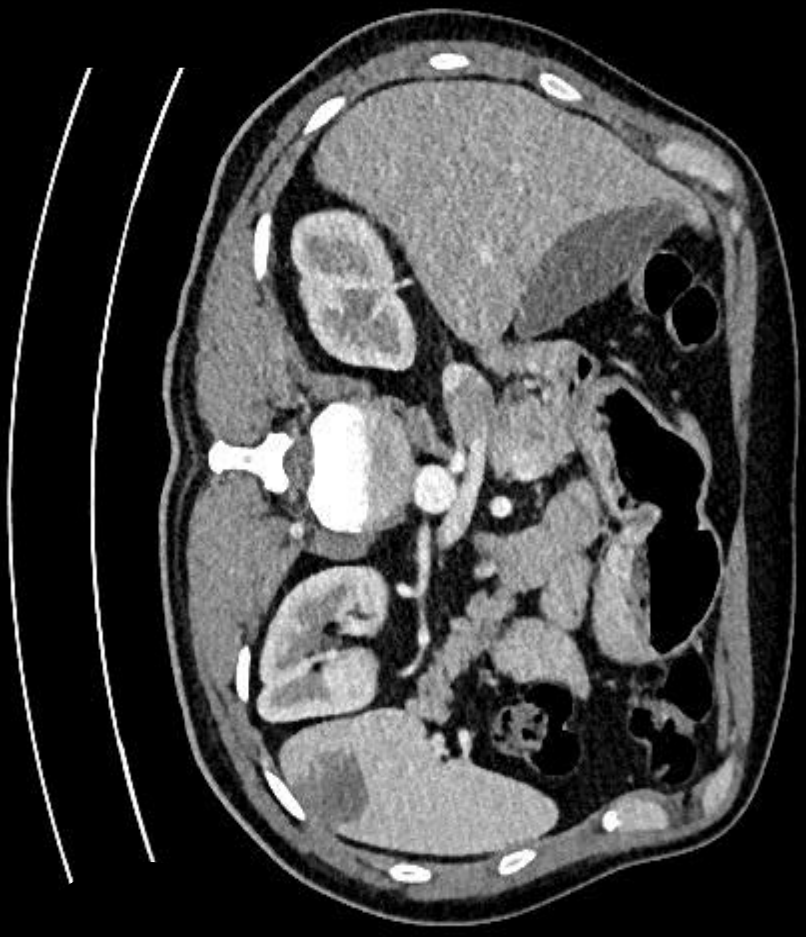
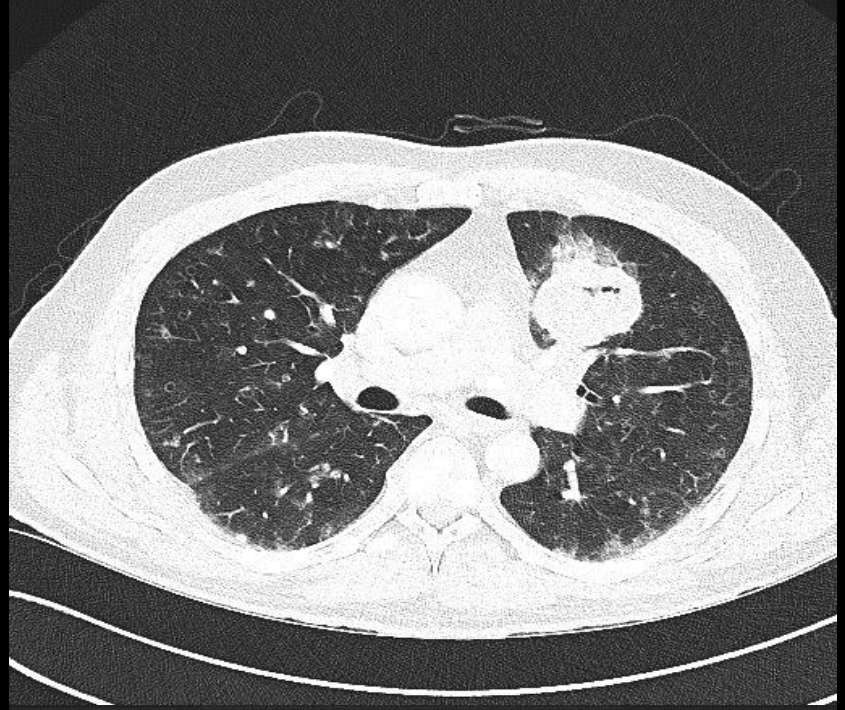
- Scheduled for TI-CE

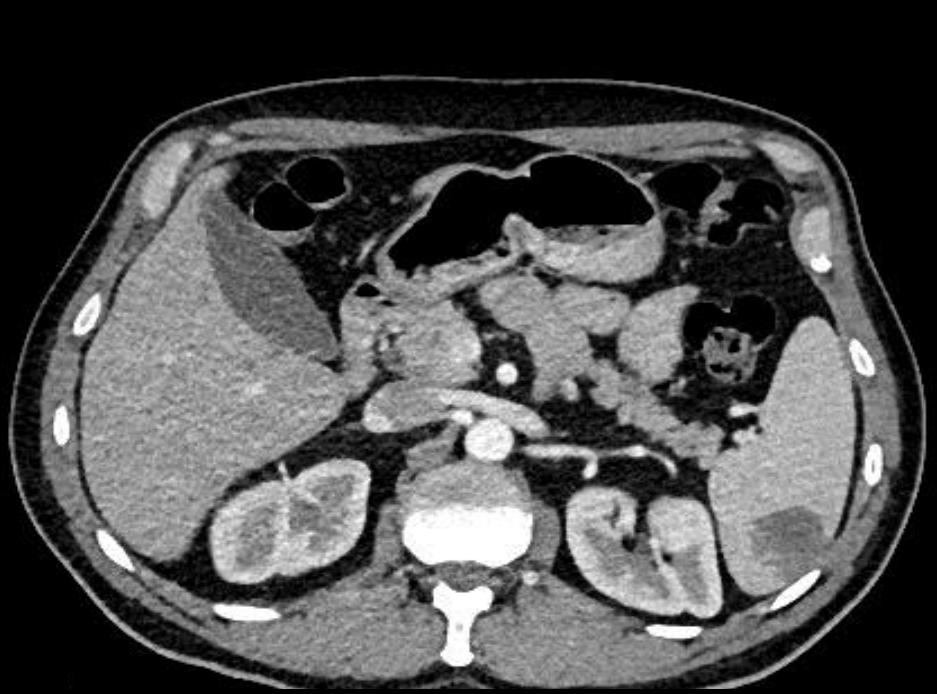
Pre Chemo



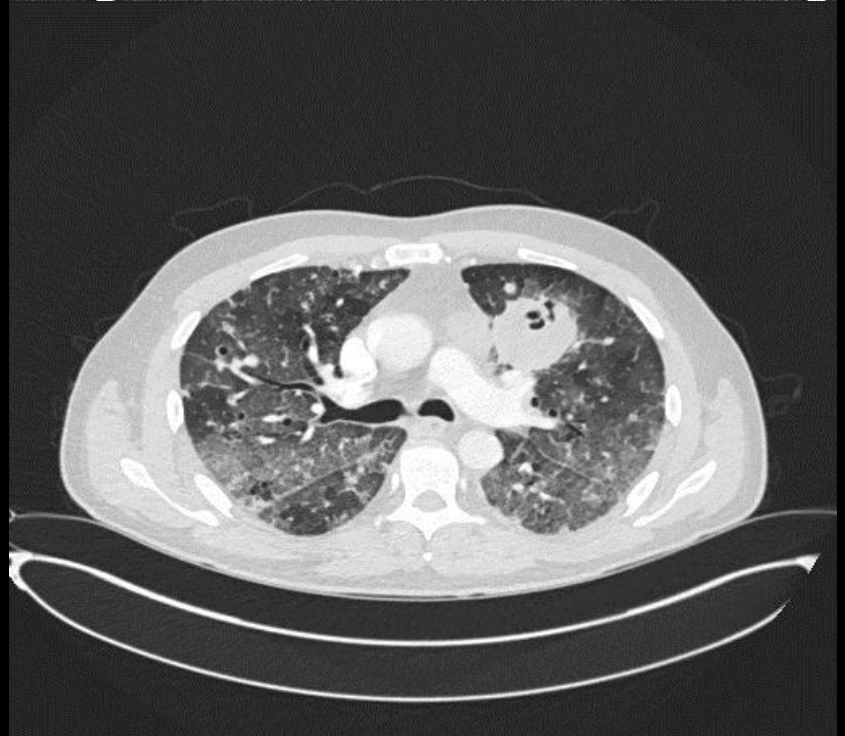


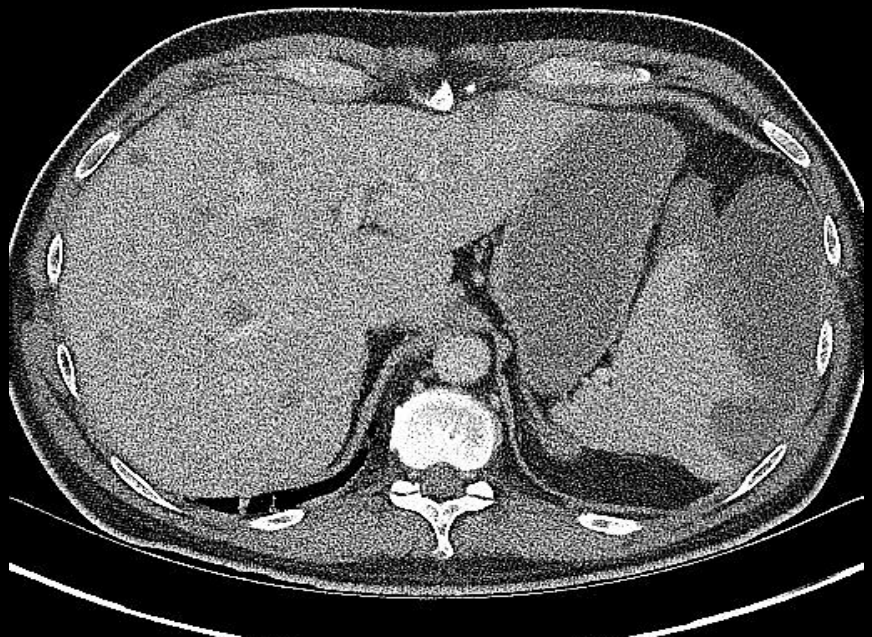
Pre Chemo





Post Chemo





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- Check at 6 months symptomatic with SOB.
  => Lung, liver, spleen, kidney, multiple brain metastases
  => HCG 4.606 U/l, AFP 3.1 ng/ml, LDH 702 U/l
- Scheduled for TI-CE, just successfully completed HDCT No 2

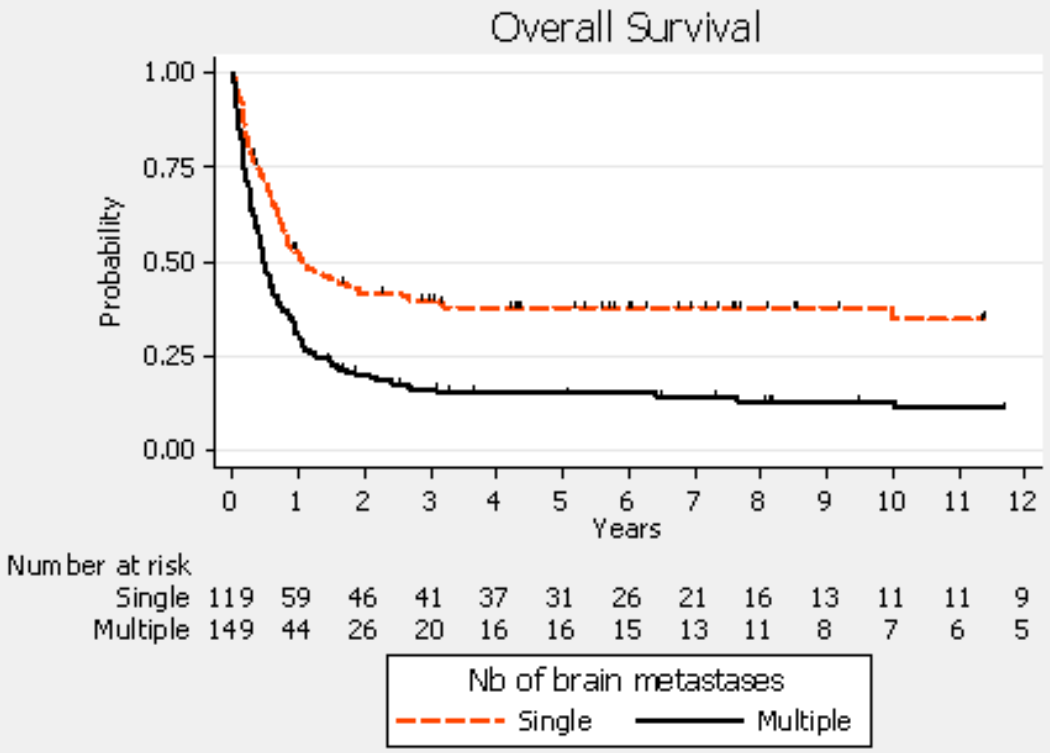
VOLUME 28 · NUMBER 33 · NOVEMBER 20 2010

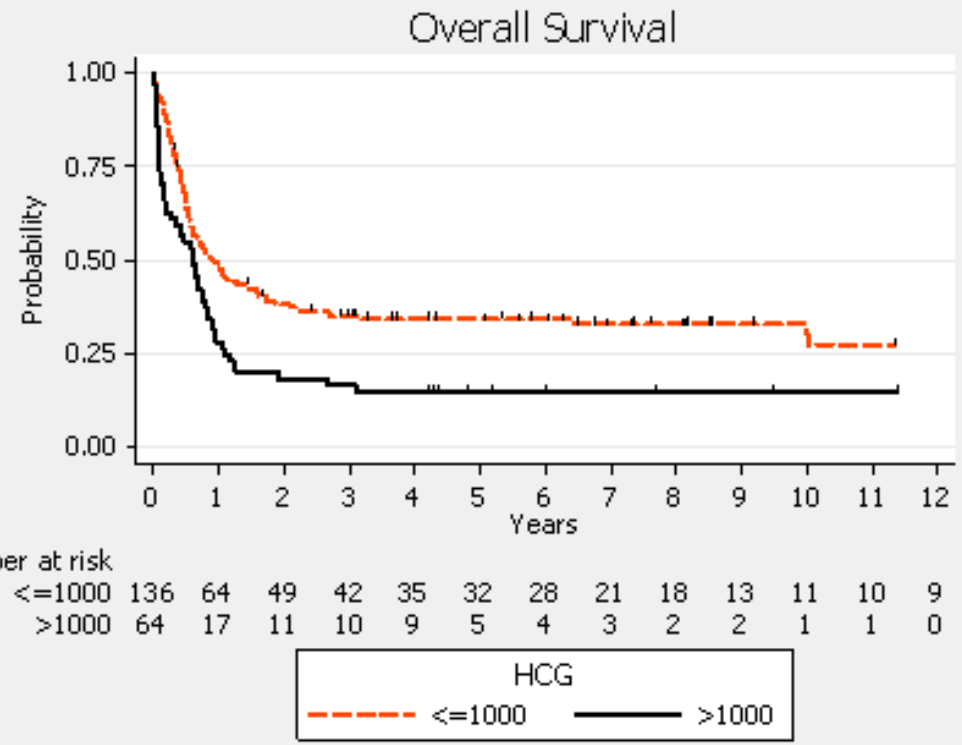
JOURNAL OF CLINICAL ONCOLOGY

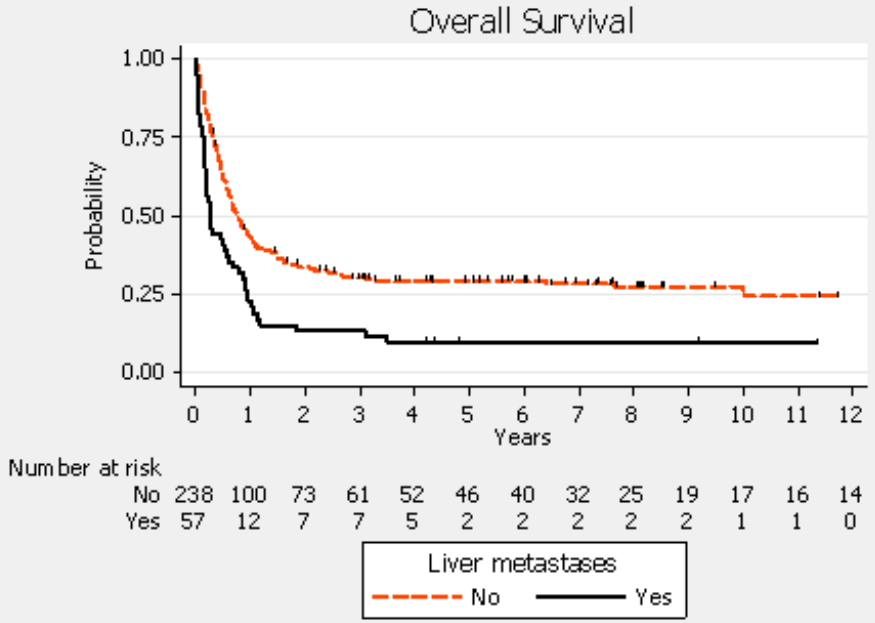
ORIGINAL REPORT

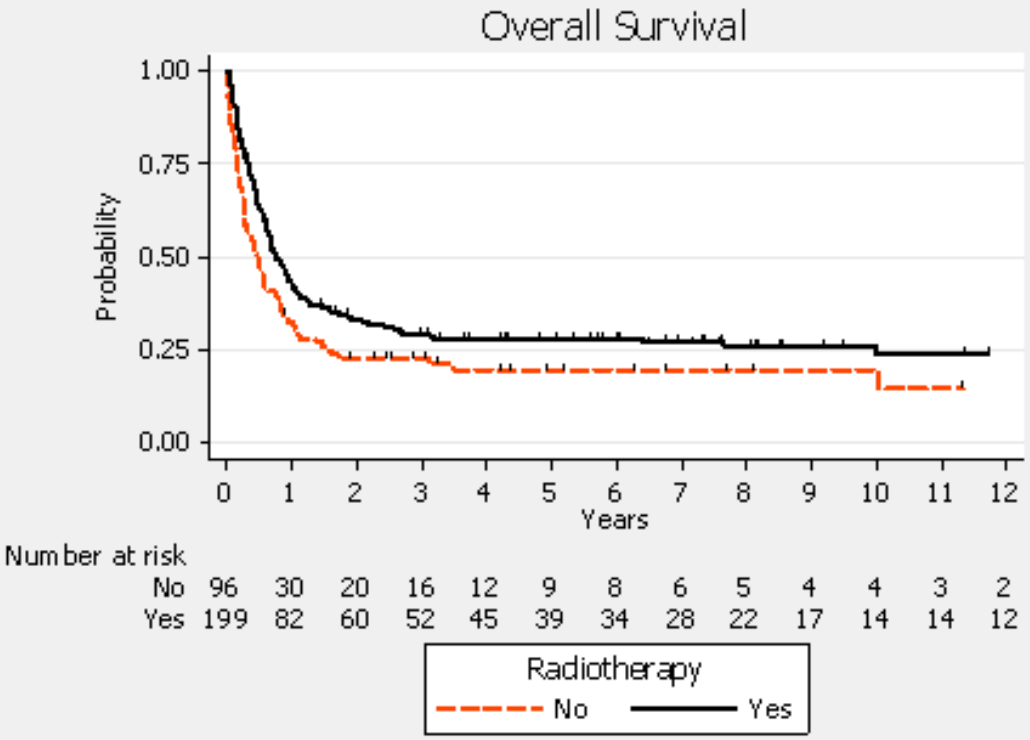
Table 4. Prognostic Score for Patients With Nonseminoma and Seminoma

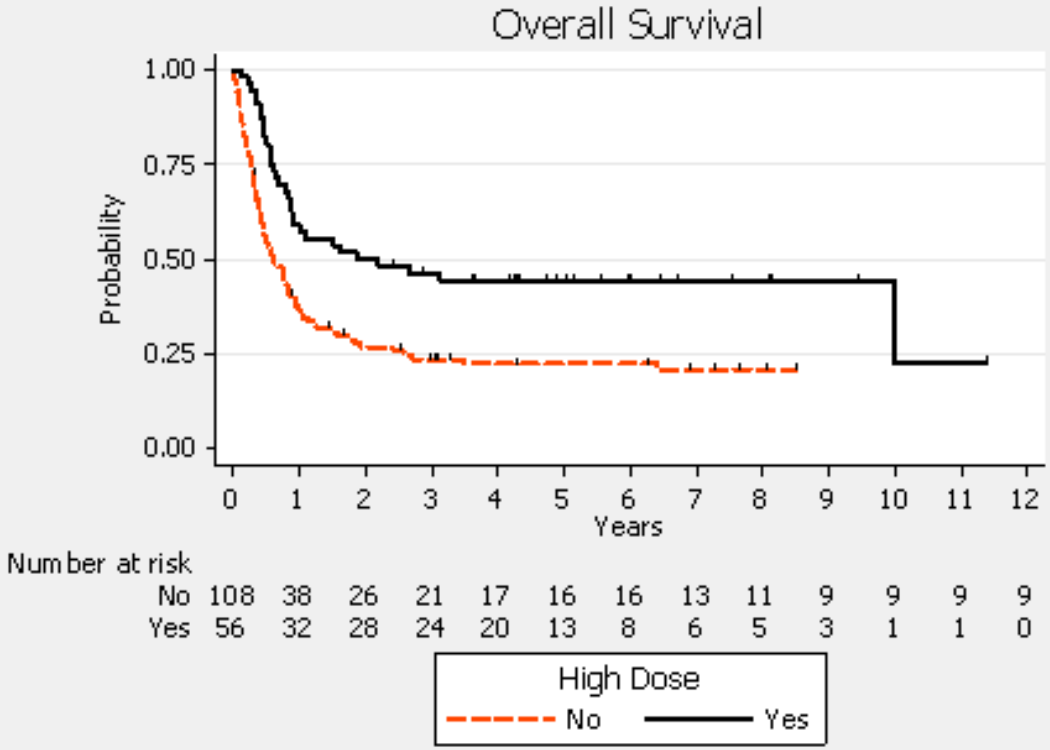
Parameter	Score Points				
	0	1	2	3	Score
Primary site	Gonadal	Extragonadal	—	Mediastinal nonseminoma	
Prior response	CR/PRm−	PRm+/SD	PD	—	
PFI, months	> 3	≤ 3	—	—	
AFP salvage	Normal	≤ 1,000	> 1,000	—	
HCG salvage	≤ 1,000	> 1,000	—	—	
LBB	No	Yes	—	—	


Overall Survival
Probability
1.00
0.75
0.50
0.25
0.00
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
Single 119 59 46 41 37 31 26 21 16 13 11 11 9
Multiple 149 44 26 20 16 16 15 13 11 8 7 6 5
Nb of brain metastases
Single
Multiple


Overall Survival
Probability
1.00
0.75
0.50
0.25
0.00
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
<=1000 136 64 49 42 35 32 28 21 18 13 11 10 9
>1000 64 17 11 10 9 5 4 3 2 2 1 1 0
HCG
<=1000
>1000


Overall Survival
Probability
1.00
0.75
0.50
0.25
0.00
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
No 238 100 73 61 52 46 40 32 25 19 17 16 14
Yes 57 12 7 7 5 2 2 2 2 2 1 1 0
Liver metastases
No
Yes


Overall Survival
Probability
1.00
0.75
0.50
0.25
0.00
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
No 96 30 20 16 12 9 8 6 5 4 4 3 2
Yes 199 82 60 52 45 39 34 28 22 17 14 14 12
Radiotherapy
No
Yes


Overall Survival
Probability
1.00
0.75
0.50
0.25
0.00
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
No 108 38 26 21 17 16 16 13 11 9 9 9 9
Yes 56 32 28 24 20 13 8 6 5 3 1 1 0
High Dose
No
Yes

Patient No 3

- 1988 Diagnosis of a non-seminoma (embryonal plus teratoma),
  Orchiectomy and primary lymphadenectomy $_{p}T_{1}\ _{p}N_{1}\ M_{0}$

  Two cycles of adjuvant cisplatin, etoposide, bleomycin
- 2013 Extensive abdominal relapse with AFP elevation

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

late relapse of seminoma and non-seminoma

Some discussions circled around the optimal definition of late relapse. There was a clear vote that the term late relapse should be limited to relapses occurring 2 years or later after full cisplatin-based chemotherapy. This definition excludes patients who relapse after adjuvant treatment or during surveillance who are usually cured by chemotherapy alone. Patients with late relapse represent a rare subgroup with an adverse prognosis as well as a high frequency of teratoma and/or non-GCC elements, who will have to be managed differently than other cohorts with GCC relapses (supplementary material S25, available at *Annals of Oncology* online). Patients with resectable late relapse should undergo immediate surgical removal of all tumor manifestations at an experienced reference center irrespective of serum tumor marker levels [62, 63]. No consensus could be achieved, however, on the management of unresectable late relapse, although the majority recommended CDCT (supplementary material S26, available at *Annals of Oncology* online) [64].

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

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  Two cycles of adjuvant cisplatin, etoposide, bleomycin
- 2013 Extensive abdominal relapse with AFP elevation
  => resection of local visceral surgeon
  => extensive surgery with R2 resection of undiff. tumor
  => transient normalization of AFP, but extensive post-OP complications
  => referred with rising AFP 295 ng/ml


順路
THIS WAY

Paclitaxel, Ifosfamide, and Cisplatin Second-Line Therapy for Patients With Relapsed Testicular Germ Cell Cancer

By Robert J. Motzer, Joel Sheinfeld, Madhu Mazumdar, Manjit Bains, Tania Mariani, Jennifer Bacik, Dean Bajorin, and George J. Bosl

Table 4. Characteristics of Patients Who Experienced Late Relapse to First-Line Therapy

Patient No.	Time to Relapse (years)	First-Line Therapy	Metastatic Sites	Elevated Pretreatment Markers	Response to TIP	Status	Survival Time from TIP (months)
1	3.0	Etoposide plus cisplatin	Lung plus retroperitoneum	AFP	Complete	Alive, NED	38+
2	3.2	Bleomycin, etoposide plus cisplatin	Retroperitoneum	HCG, LDH	Complete	Alive, NED	12+
3	6.7	VAB-6 + high-dose carboplatin plus etoposide	Liver plus retroperitoneum	None	Complete	Alive, NED	21+
4	8.8	Etoposide plus carboplatin	Retroperitoneum	AFP	Incomplete	Alive, NED	39+
5	11.8	Bleomycin, etoposide plus cisplatin	Retroperitoneum	AFP, LDH	Incomplete	Dead	25
6	12.7	VAB-6	Retroperitoneum bone, plus liver	AFP, LDH	Incomplete	Dead	9

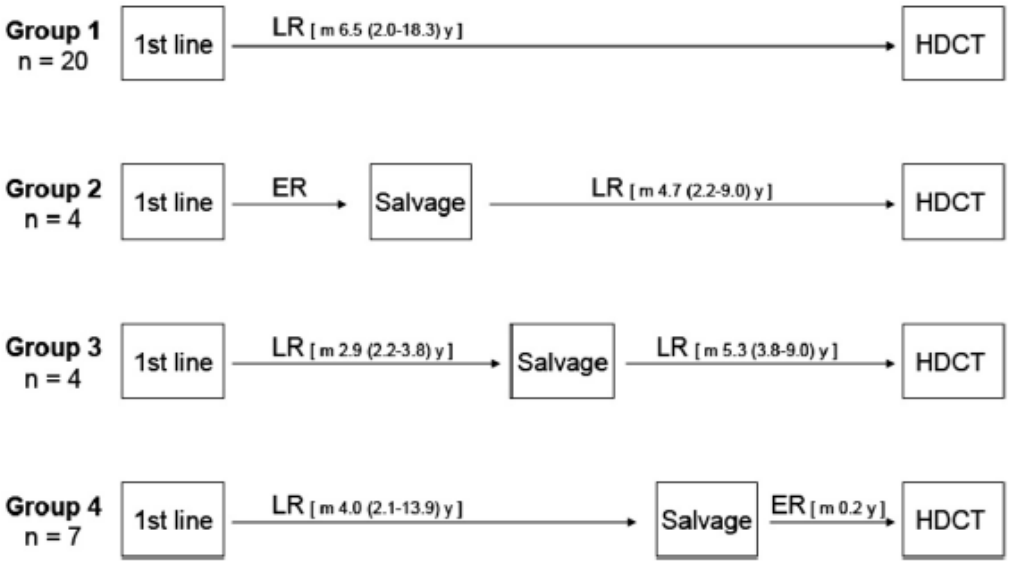
Abbreviations: AFP, alfa fetoprotein; NED, no evidence of disease; VAB-6, cisplatin, vinblastine, bleomycin, cyclophosphamide plus actinomycin-D; LDH, lactate dehydrogenase.

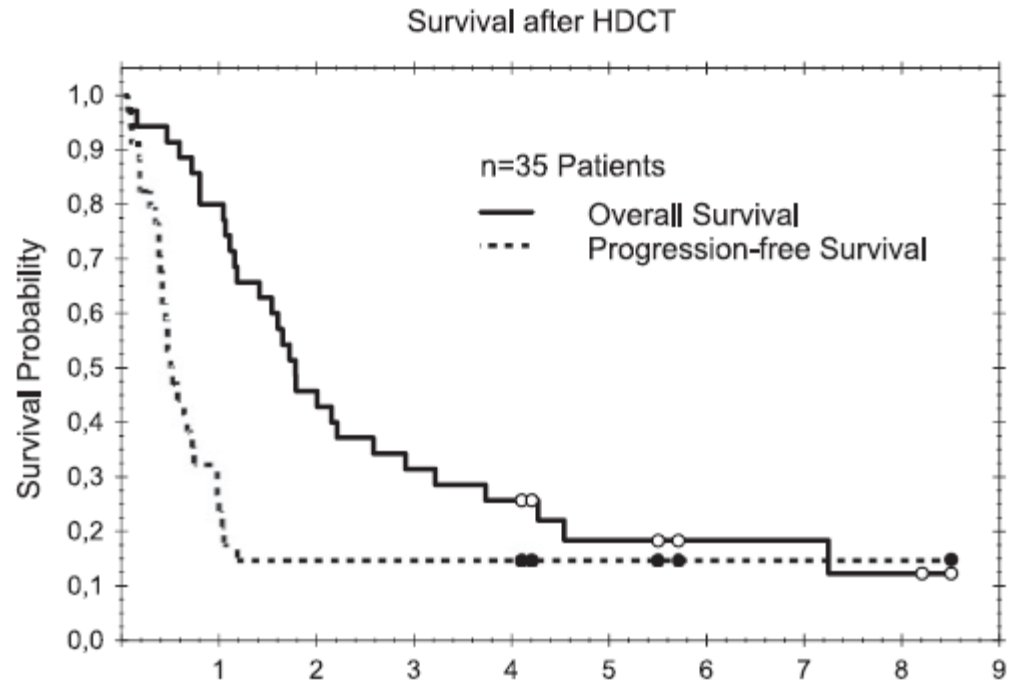
J Clin Oncol 18:2413-2418.

High Dose Chemotherapy as Salvage Treatment for Unresectable Late Relapse Germ Cell Tumors

Anja Lorch,* Oliver Rick, Thomas Wündisch, Jörg-Thomas Hartmann, Carsten Bokemeyer and Jörg Beyer

From the Departments of Hematology and Oncology, Universitätsklinikum Giessen und Marburg GmbH (AL, TW), Marburg, Vivantes Klinikum Am Urban (UB), Berlin, Klinik Reinhardshöhe (OR), Bad-Wildungen, Universitätsklinikum (JTH), Tübingen and Universitätskrankenhaus Eppendorf (CB), Hamburg, Germany





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- 2013 Extensive abdominal relapse with AFP elevation
  => resection of local visceral surgeon
  => extensive surgery with R2 resection of undiff. tumor
  => transient normalization of AFP, but extensive post-OP complications
  => referred with rising AFP 295 ng/ml
- 2013 TI-CE chemotherapy with normalization of AFP remains free of progression for about one year

Third-line (palliative) regimens

Oechsle/Bokemeyer (2011) "GOP"

Oxaliplatin	130 mg/m^2	Day 1
Gemcitabin	800 mg/m^2	Day 1 & 8
Paclitaxel	80 mg/m^2	Day 1 & 8

Nicolai/Necchi (2009) "CGP"

Cisplatin	50 mg/m^2	Day 1 & 8
Gemcitabin	800 mg/m^2	Day 1 & 8
Paclitaxel	80 mg/m^2	Day 1 & 8

Einhorn (2007) "GP"

Gemcitabin	1000 mg/m^2	Day 1, 8 & 15
Paclitaxel	100 mg/m^2	Day 1, 8 & 15

Cooper/Einhorn (1995) "Oral Etoposide"

Etoposide	50 mg/m^2	Day 1-14

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