UniversitätsSpital Zürich

Hochdosistherapie bei Hodenkrebs

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- Primärtherapie
- Salvagetherapie

International Germ Cell Consensus Classification: A Prognostic Factor-Based Staging System for Metastatic Germ Cell Cancers

By the International Germ Cell Cancer Collaborative Group

***J Clin Oncol* 15:594-603.**

RISK CLASSIFICATION

Risk Status	Nonseminoma	Seminoma
Good Risk Overall Survival > 90 %	Testicular or retroperitoneal primary tumor and No nonpulmonary visceral metastases and Good markers- all of: AFP < 1,000 ng/mL hCG < 5,000 iu/L LDH < 1.5 x upper limit of normal	Any primary site and No nonpulmonary visceral metastases and Normal AFP Any HCG Any LDH
Intermediate Risk Overall Survival ~ 78 %	Testicular or retroperitoneal primary tumor and No nonpulmonary visceral metastases and Intermediate markers- any of: AFP 1,000-10,000 ng/mL hCG 5,000-50,000 iu/L LDH 1.5-10 x upper limit of normal	Any primary site and Nonpulmonary visceral metastases and Normal AFP Any HCG Any LDH
Poor Risk Overall Survival ~ 45 %	Mediastinal primary tumor or Nonpulmonary visceral metastases or Poor markers- any of: AFP > 10,000 ng/mL hCG > 50,000 iu/L LDH > 10 x upper limit of normal	No patients classified as poor prognosis

Surival after first-treatment

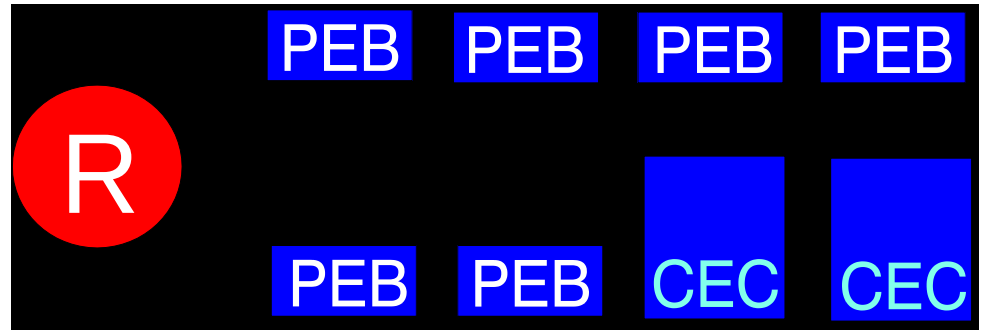
	Risk Groups			
(299 Patients)	good	inter-mediate	poor	all
1977-1986	95%	74%	37%	76%
1987-1996	94%	87%	66%	88%

Sonneveld et al., Cancer 2001, 91: 1304

Randomized trials using upfront HDCT

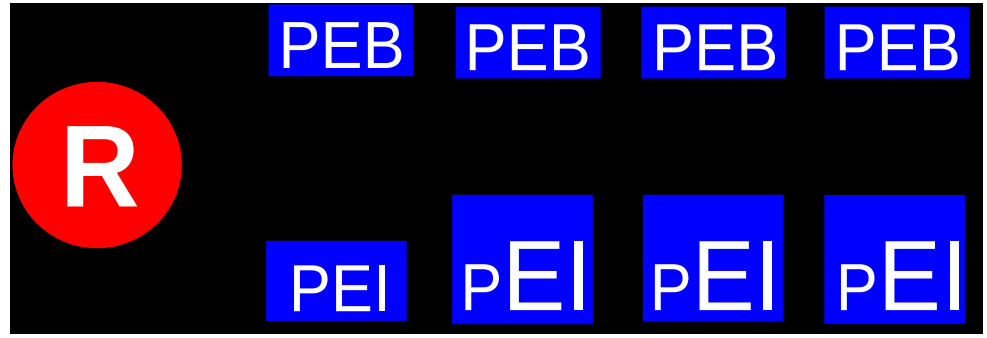
n=219, JCO 2007, Motzer et al.

„Intergroup trial“ USA
Started 1997
Published 2007
No benefit from upfront HDCT



n=131, Ann Oncol 2011, Daugaard et al.

„EORTC GU“ Europe
Started 1999
Published 2011
No benefit from upfront HDCT



VOLUME 25 · NUMBER 3 · JANUARY 20 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Phase III Randomized Trial of Conventional-Dose Chemotherapy With or Without High-Dose Chemotherapy and Autologous Hematopoietic Stem-Cell Rescue As First-Line Treatment for Patients With Poor-Prognosis Metastatic Germ Cell Tumors

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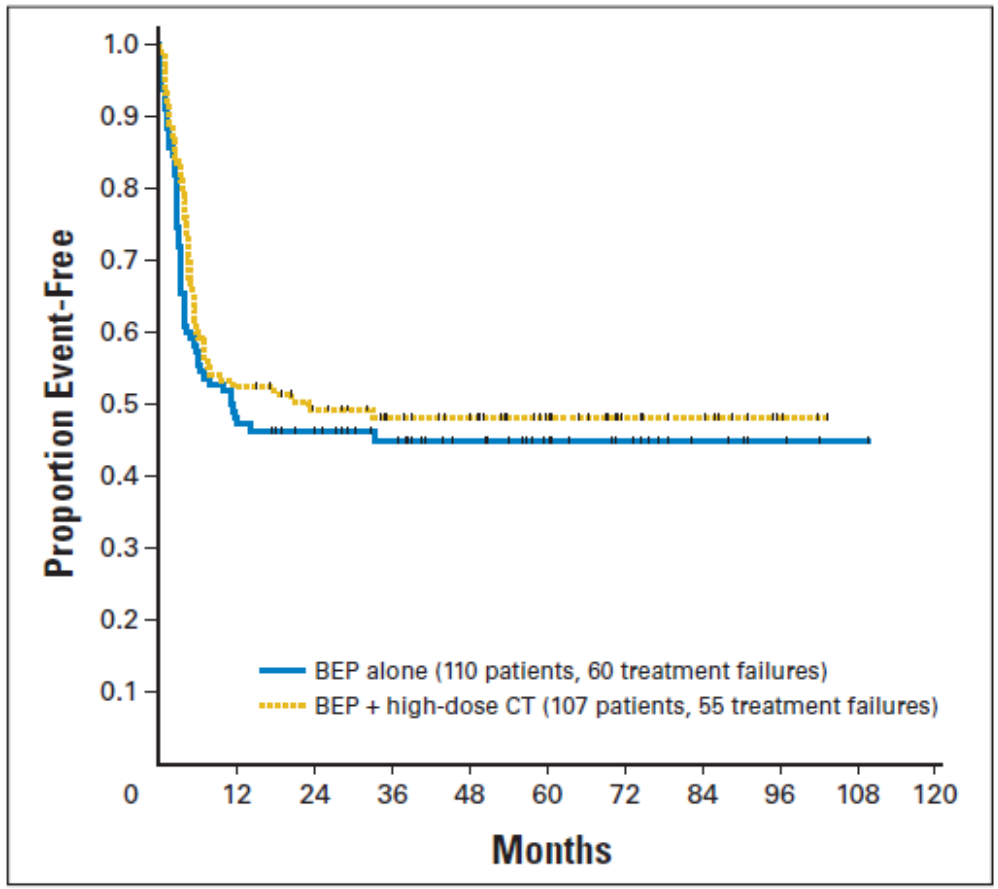
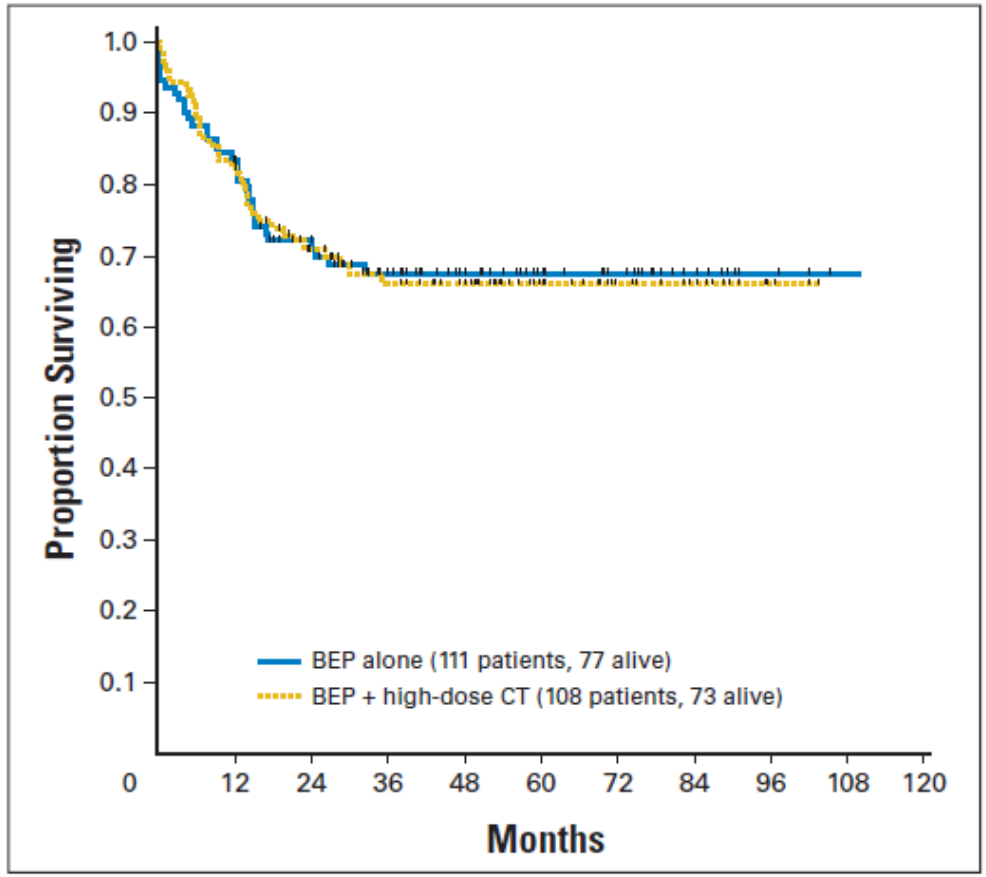
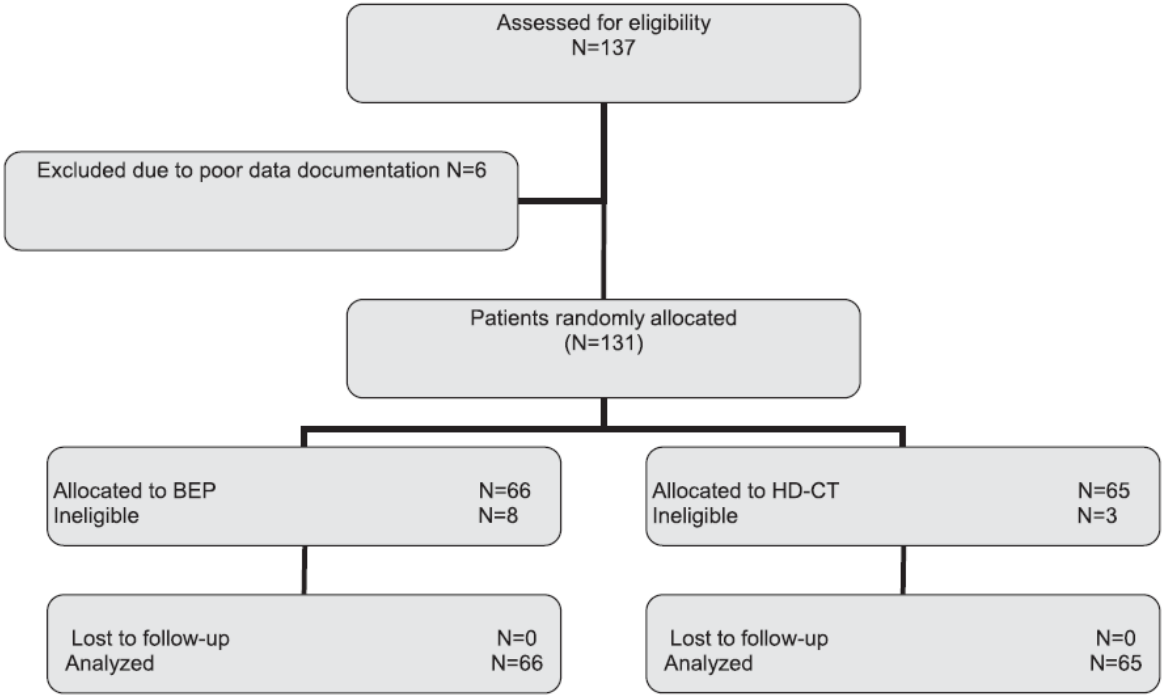


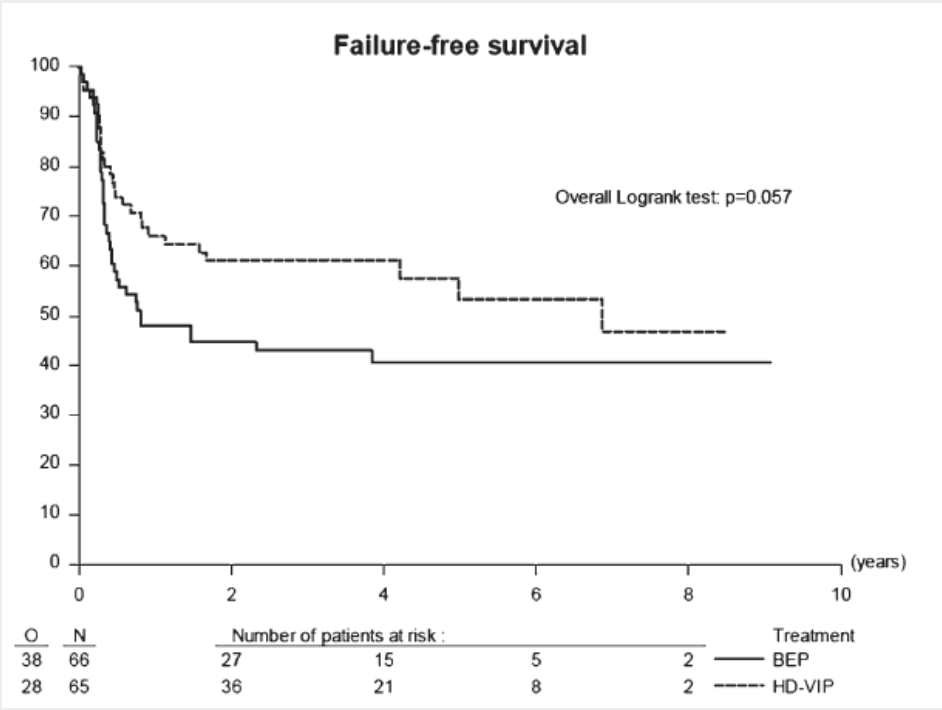


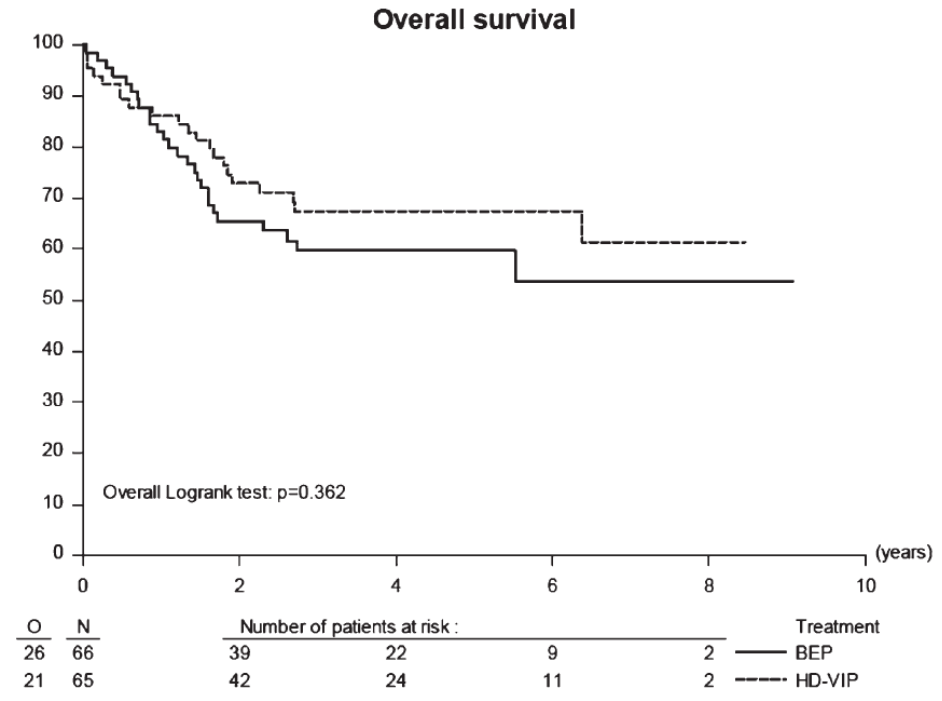
A randomized phase III study comparing standard dose BEP with sequential high-dose cisplatin, etoposide, and ifosfamide (VIP) plus stem-cell support in males with poor-prognosis germ-cell cancer. An intergroup study of EORTC, GTCSG, and Grupo Germinal (EORTC 30974)

G. Daugaard[1]*, I. Skoneczna[2], N. Aass[3], R. De Wit[4], M. De Santis[5], H. Dumez[6], S. Marreaud[7], L. Collette[7], J. R. G. Lluch[8], C. Bokemeyer[9] & H. J. Schmoll[10]



Annals of Oncology 22: 1054–1061, 2011





Identification of prognostic subgroups among patients with metastatic 'IGCCCG poor-prognosis' germ-cell cancer: An explorative analysis using cart modeling*

Annals of Oncology **11**: 1115–1120, 2000.

C. Kollmannsberger,[1] C. Nichols,[2] C. Meisner,[3] F. Mayer,[1] L. Kanz[1] & C. Bokemeyer[1]

[1]*Department of Hematology/Oncology, University of Tübingen Medical Center, Germany;* [2]*Division of Hematology/Oncology, Oregon Health Science University, Oregon, USA;* [3]*Institute for Medical Information Processing, University of Tübingen, Germany*

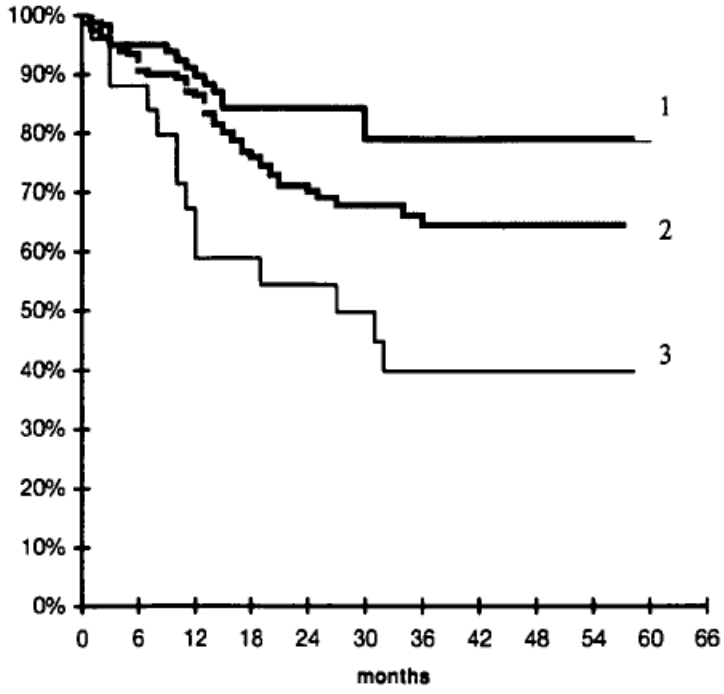
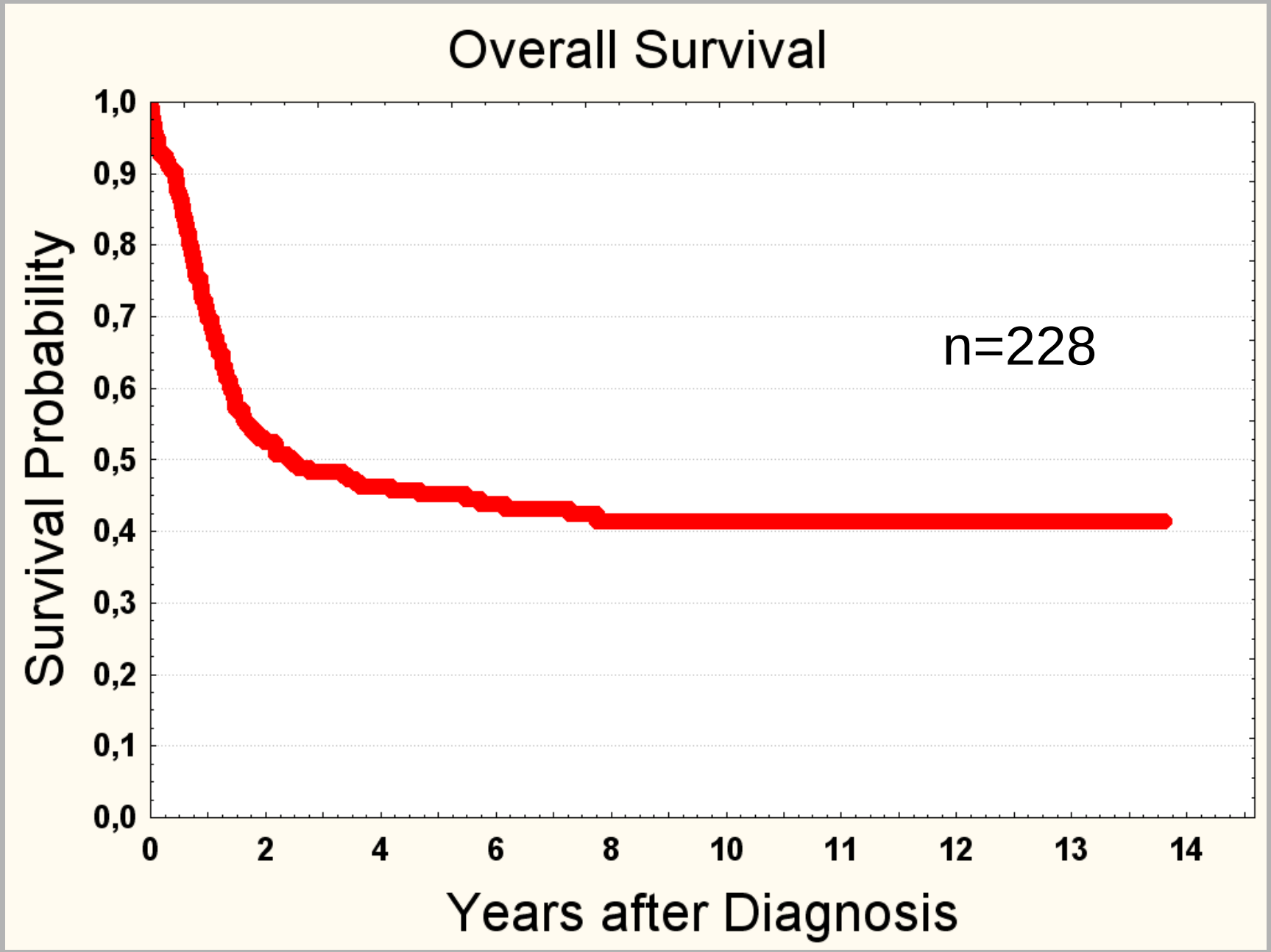
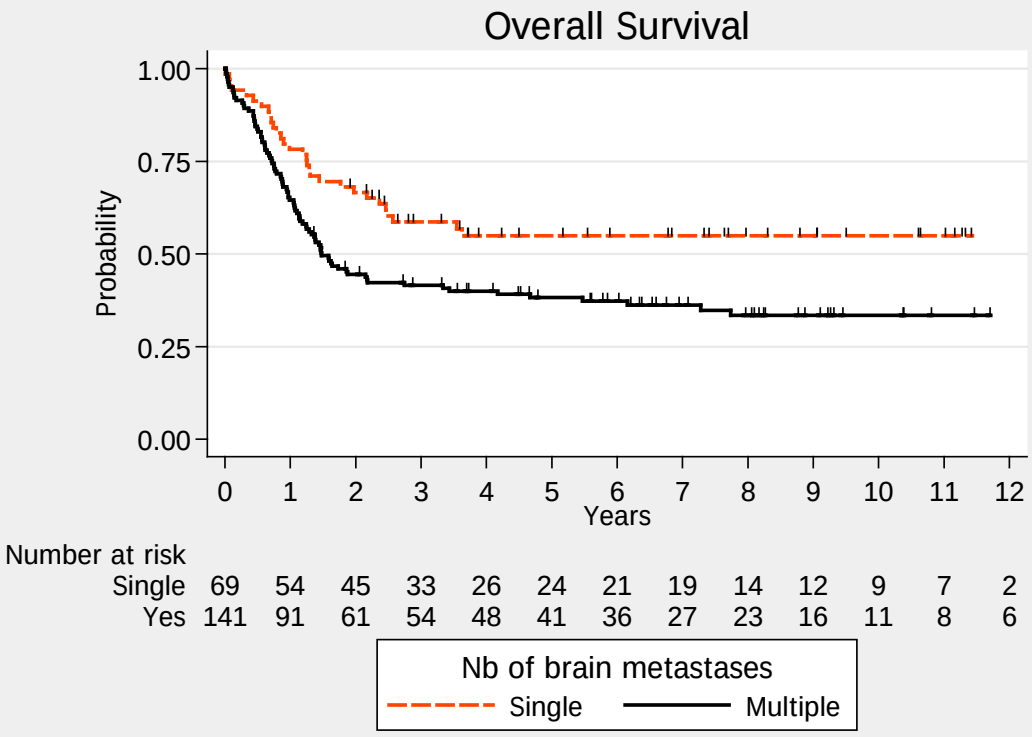


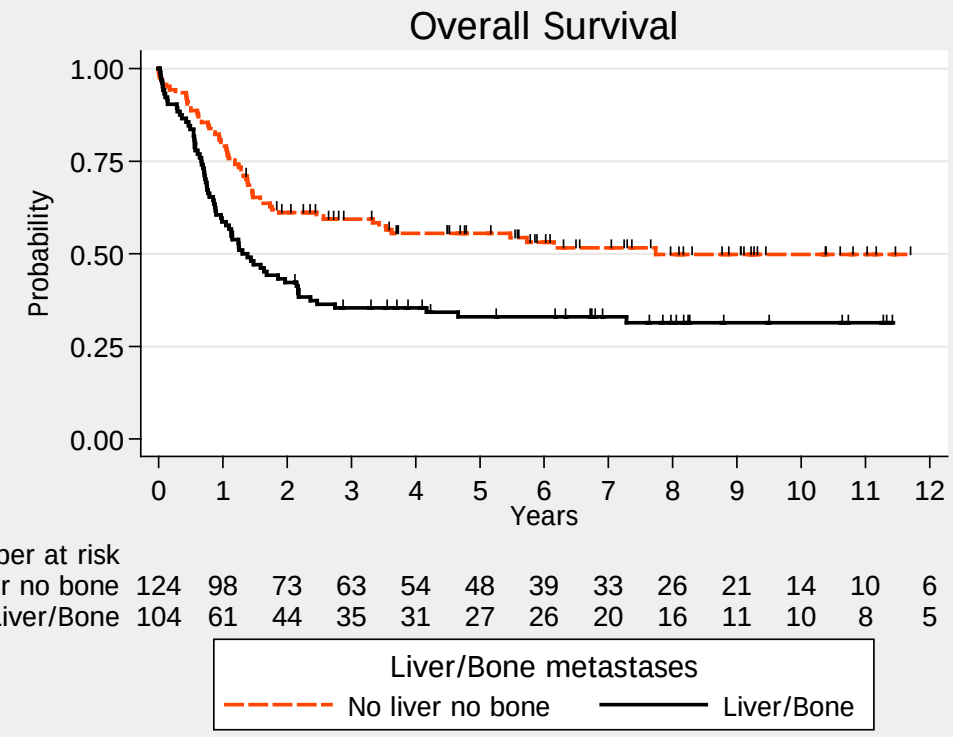
Table 3. Risk grouping for overall survival among 332 'poor prognosis' NSGCT patients based on CART analysis.

Risk group	Features	Percentage estimated two-year survival rate (95% CI)	Number of patients (% of entire population)
Good–poor	Gonadal/retroperitoneal primary site without visceral metastases	84 (76–92)	80 (24)
Intermediate–poor	Other than favorable or unfavorable	64 (52–72)	227 (68)
Poor–poor	Visceral metastases plus mediastinal primary site	49 (29–70)	25 (8)

Patients with brain metatases at initial diagnosis




Overall Survival
1.00
0.75
0.50
0.25
0.00
Probability
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
Single 69 54 45 33 26 24 21 19 14 12 9 7 2
Yes 141 91 61 54 48 41 36 27 23 16 11 8 6
Nb of brain metastases
Single
Multiple


Overall Survival
1.00
0.75
0.50
0.25
0.00
Probability
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Number at risk
No liver no bone 124 98 73 63 54 48 39 33 26 21 14 10 6
Liver/Bone 104 61 44 35 31 27 26 20 16 11 10 8 5
Liver/Bone metastases
No liver no bone
Liver/Bone

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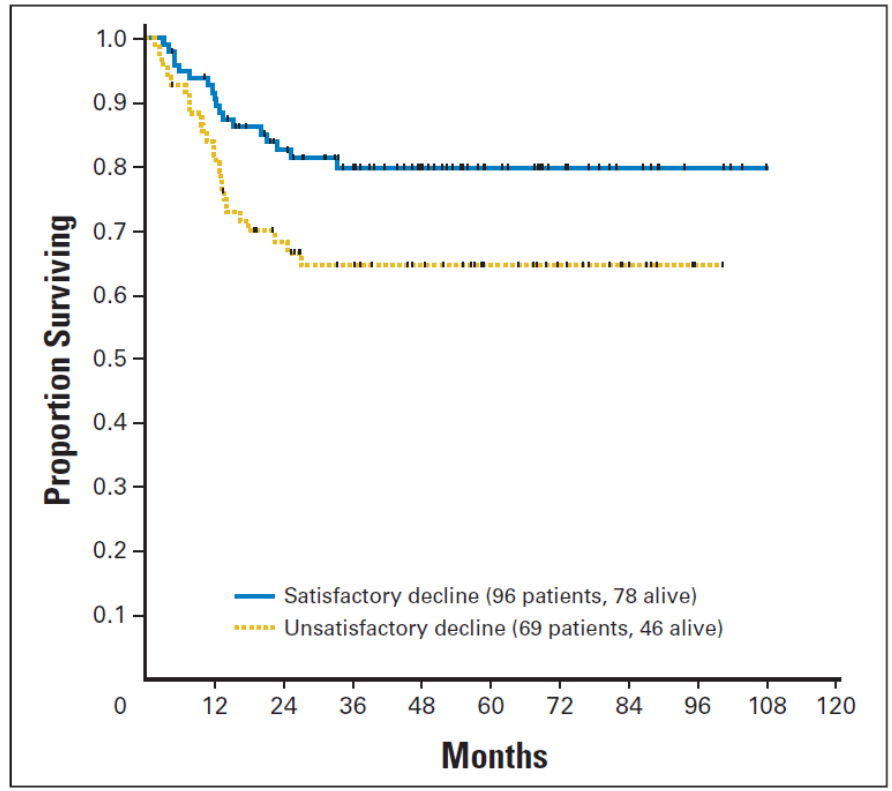
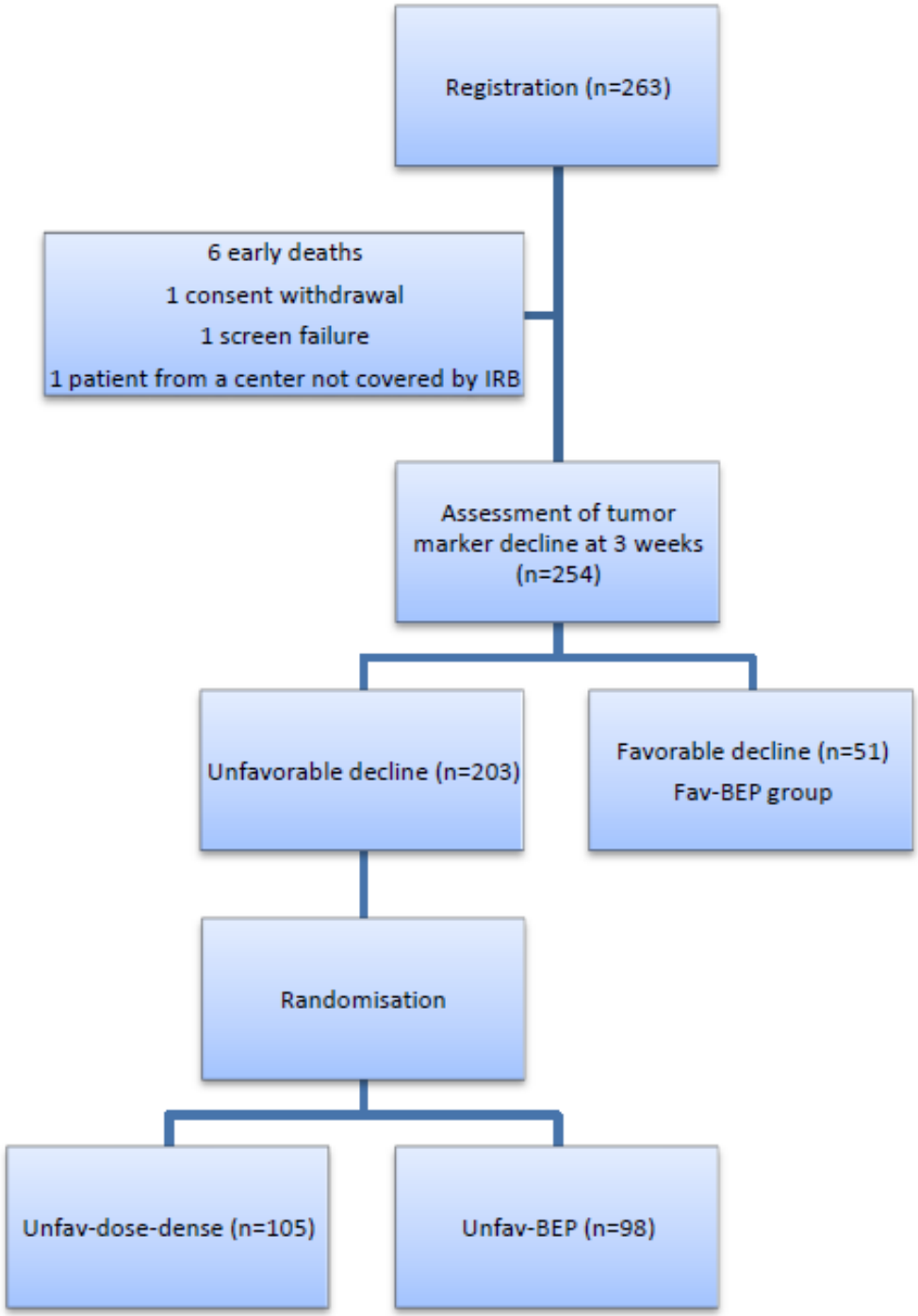


marker were included in the regression. Marker decline was defined as satisfactory if both AFP and HCG demonstrated satisfactory decline (declined to normal by the start of cycle 3 or had a half-life $\leq$ 7 days for AFP and $\leq$ 3.5 days for HCG) or if one marker had a satisfactory decline and the other was not elevated at baseline. The marker decline was unsatisfactory if one or both markers demonstrated a slow decline (half-life $>$ 7 days for AFP or $>$ 3.5 days for HCG).



GETUG ASCO 2013

BEP × 1

Cisplatin 20 mg/m²/d d1-5
Etoposide 100 mg/m²/d d1-5
Bleomycin 30 u/w

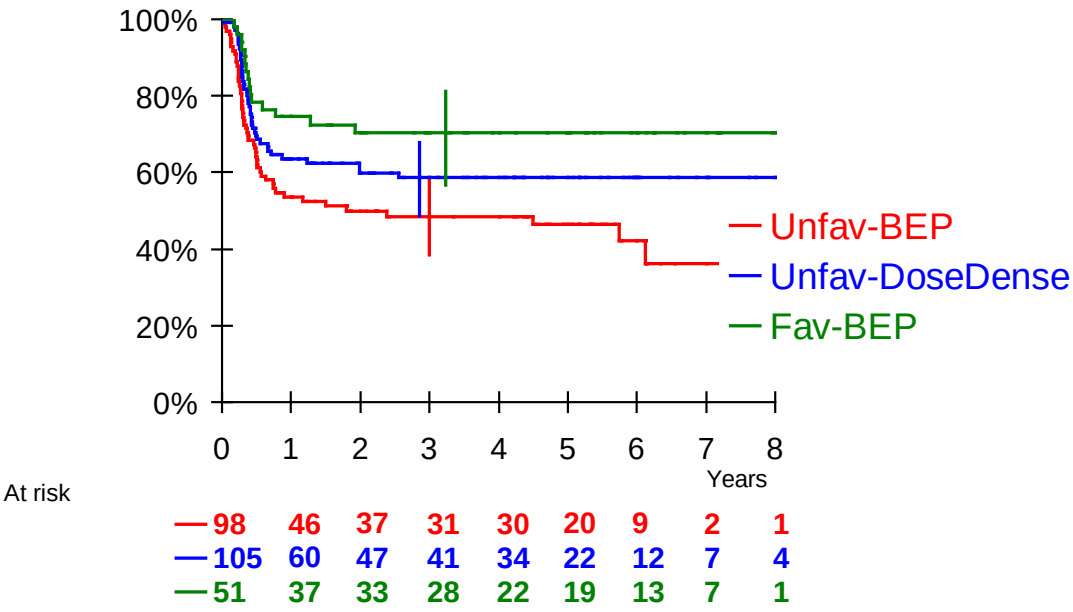
Paclitaxel-BEP + Oxaliplatin
+ G-CSF
/ 3 weeks × 2 cycles

Paclitaxel 175 mg/m² d1
BEP as above
Oxaliplatin 130 mg/m² d10
G-CSF 263 µg/d (excepted chemo days)

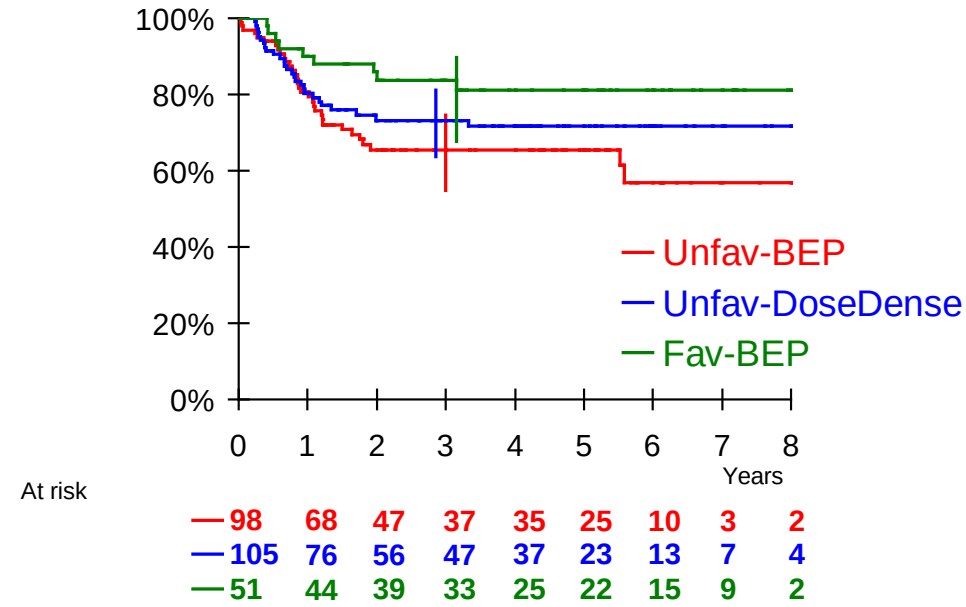
Cisplatin, Ifosfamide, Bleomycin
+ G-CSF
/ 3 weeks × 2 cycles

Cisplatin 100 mg/m² d1
Ifosfamide 2g/m² d10,12,14
Mesnum
Bleomycin 25 U/d d10-14 (continuous IV)
G-CSF as above

Progression-free Survival

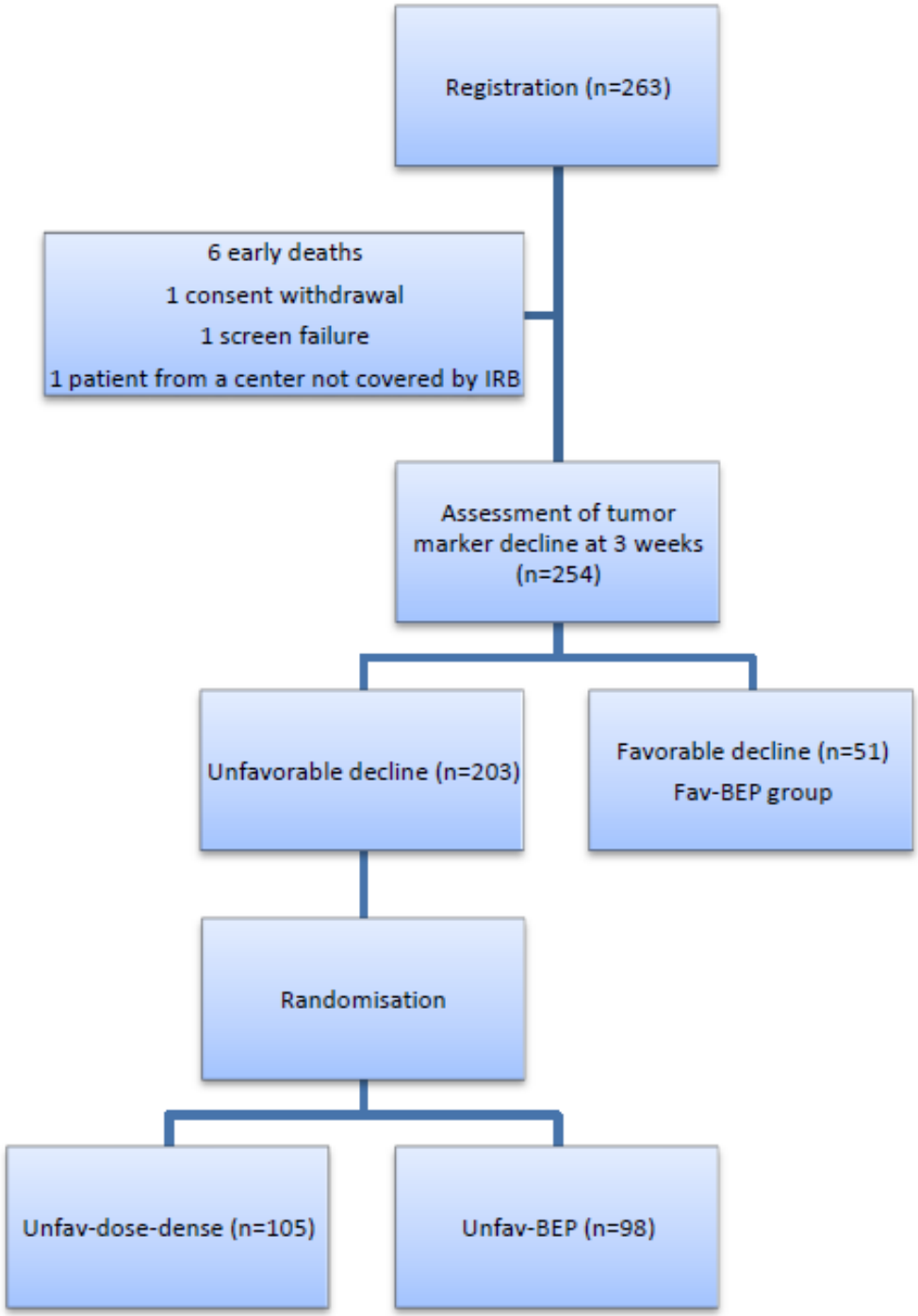


Overall Survival



Fav-BEP vs Unfav-BEP:
3-year PFS: 70% vs 48%
HR=0.66 (0.49 ; 0.88), p=0.01

Fav-BEP vs Unfav-BEP:
3-year OS: 84% vs 65%
HR=0.65 (0.45 ; 0.95), p=0.024



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Mesnum
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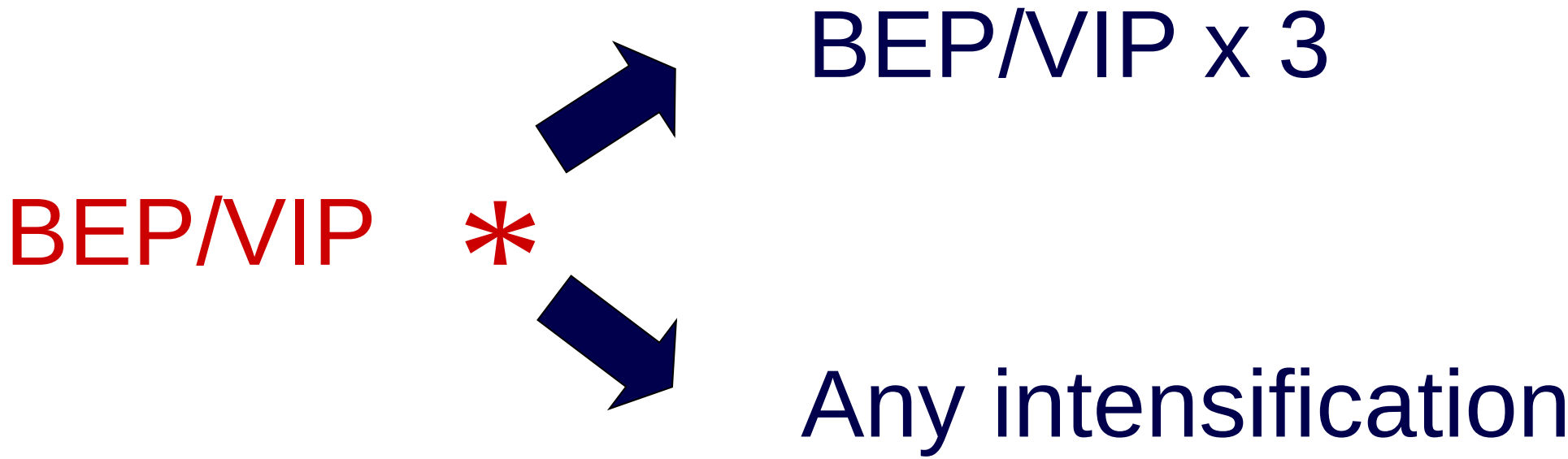
G-CSF as above



* Abfall der Tumormarker AFP / HCG

Wer könnte am meisten profitieren ?

- Patienten mit primär mediastinalen Keimzelltumoren
- Patienten mit ZNS, Leber oder Knochenmetastasen
- Patienten mit langsamen Markerabfall

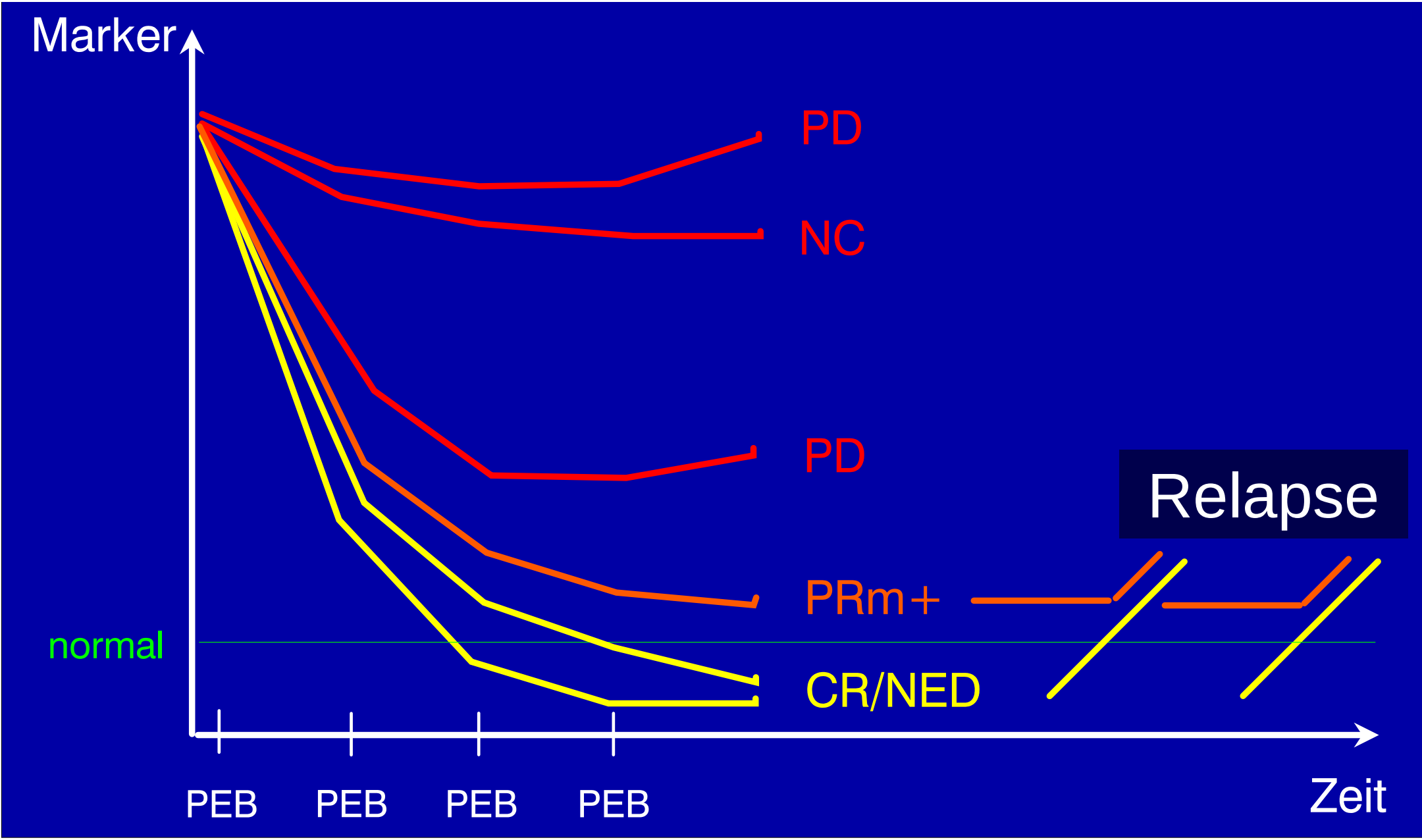
Registerstudie zur primären Hochdosis-Chemotherapie bei „poor risk“ Patienten mit metastasiertem Keimzelltumor

Hubertus Wald Tumorzentrum
Universitäres Cancer Center Hamburg

REGISTERSTUDIE ZUR PRIMÄREN HOCHDOSIS-CHEMOTHERAPIE BEI „POOR RISK“ PATIENTEN MIT METASTASIERTEM KEIMZELLTUMOR

- Primärtherapie
- Salvagetherapie

First line failures

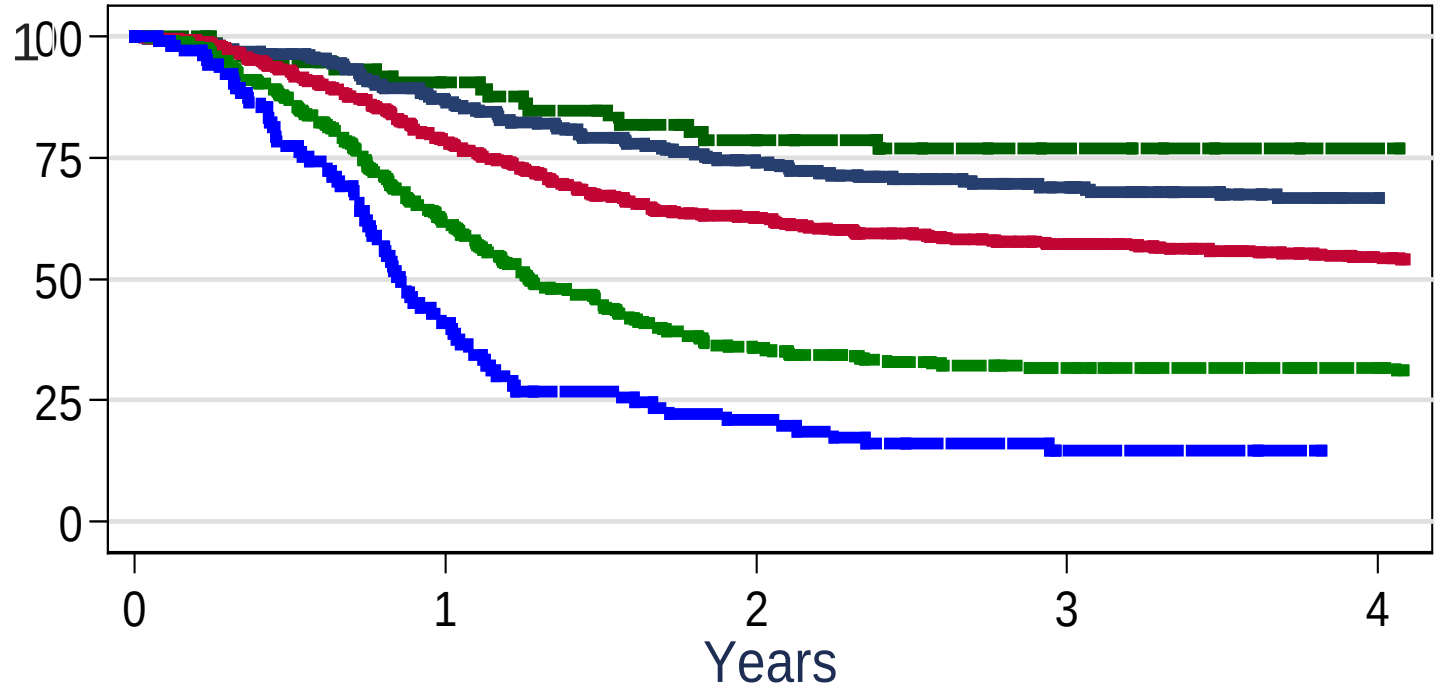


ORIGINAL REPORT
JOURNAL OF CLINICAL ONCOLOGY
VOLUME 28 · NUMBER 33 · NOVEMBER 20 2010

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

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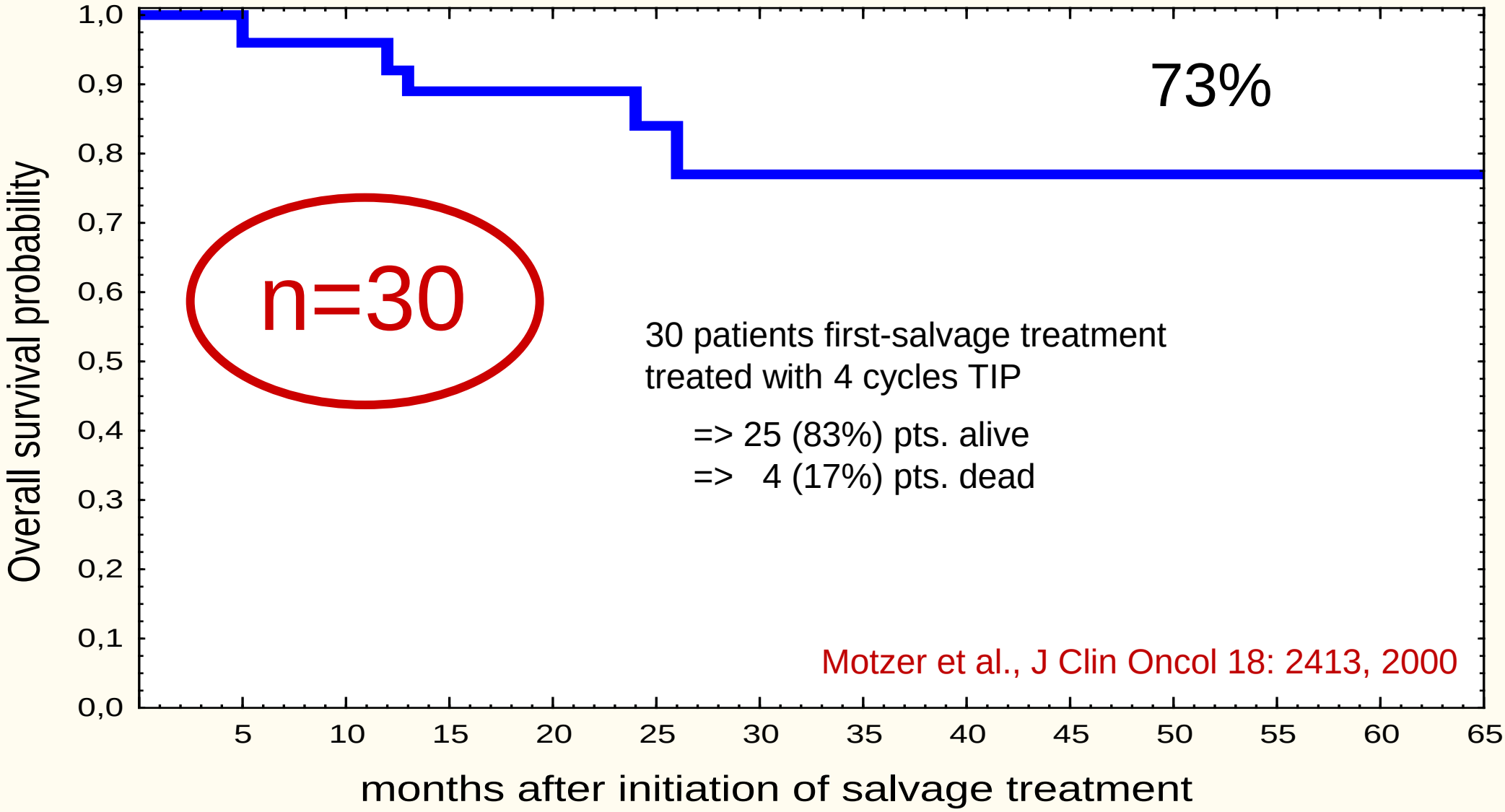
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Table 4. Prognostic Score for Patients With Nonseminoma and Seminoma

	Score Points				
Parameter	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	—	—	

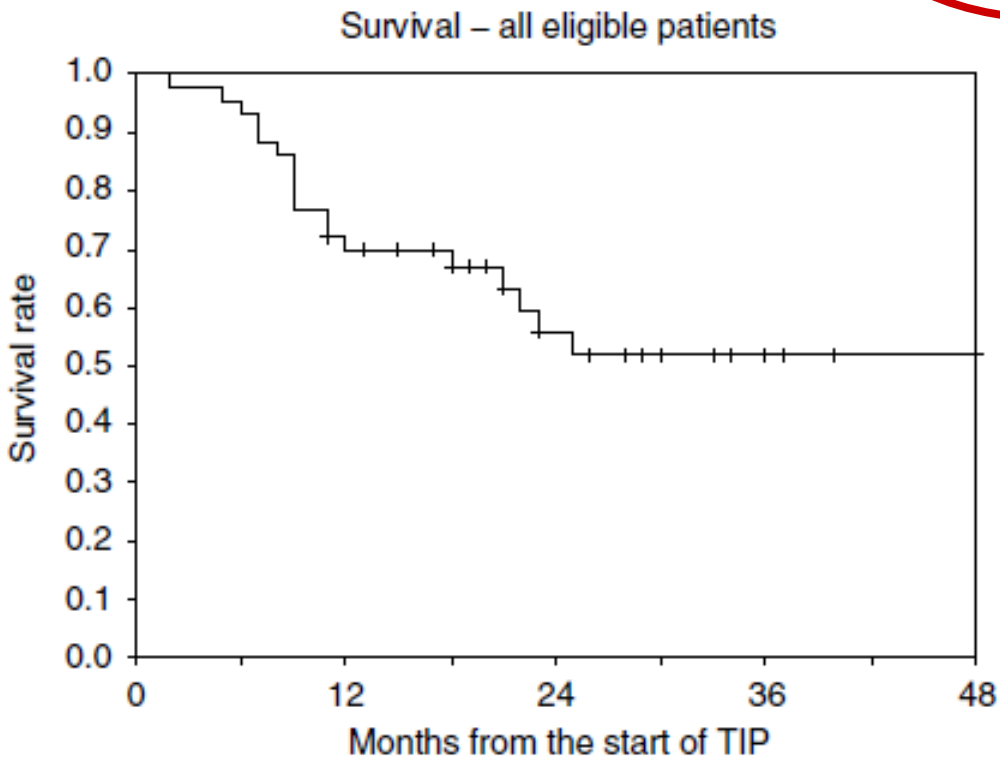
Survival after conventional-dose first-salvage treatment



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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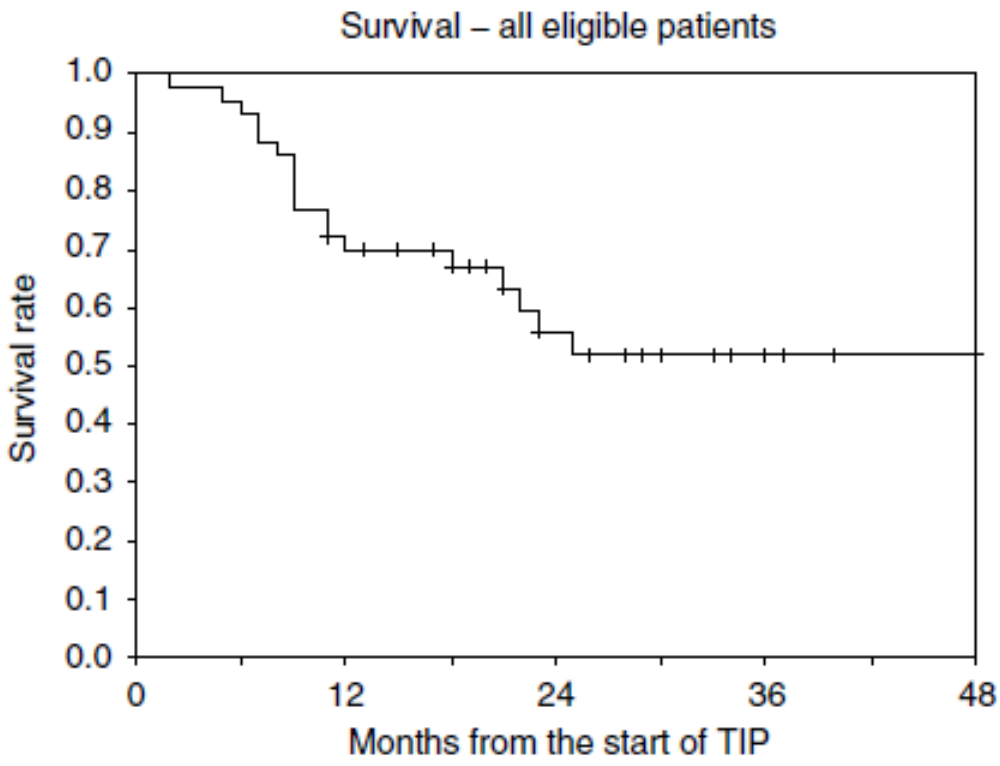

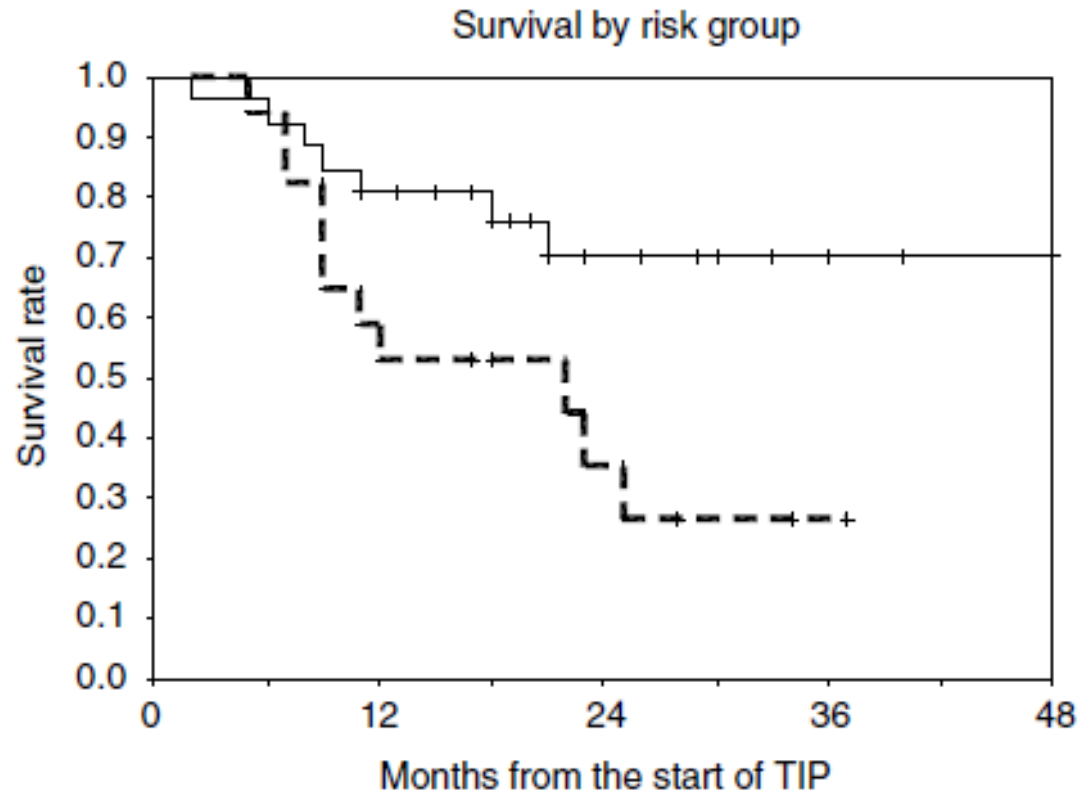

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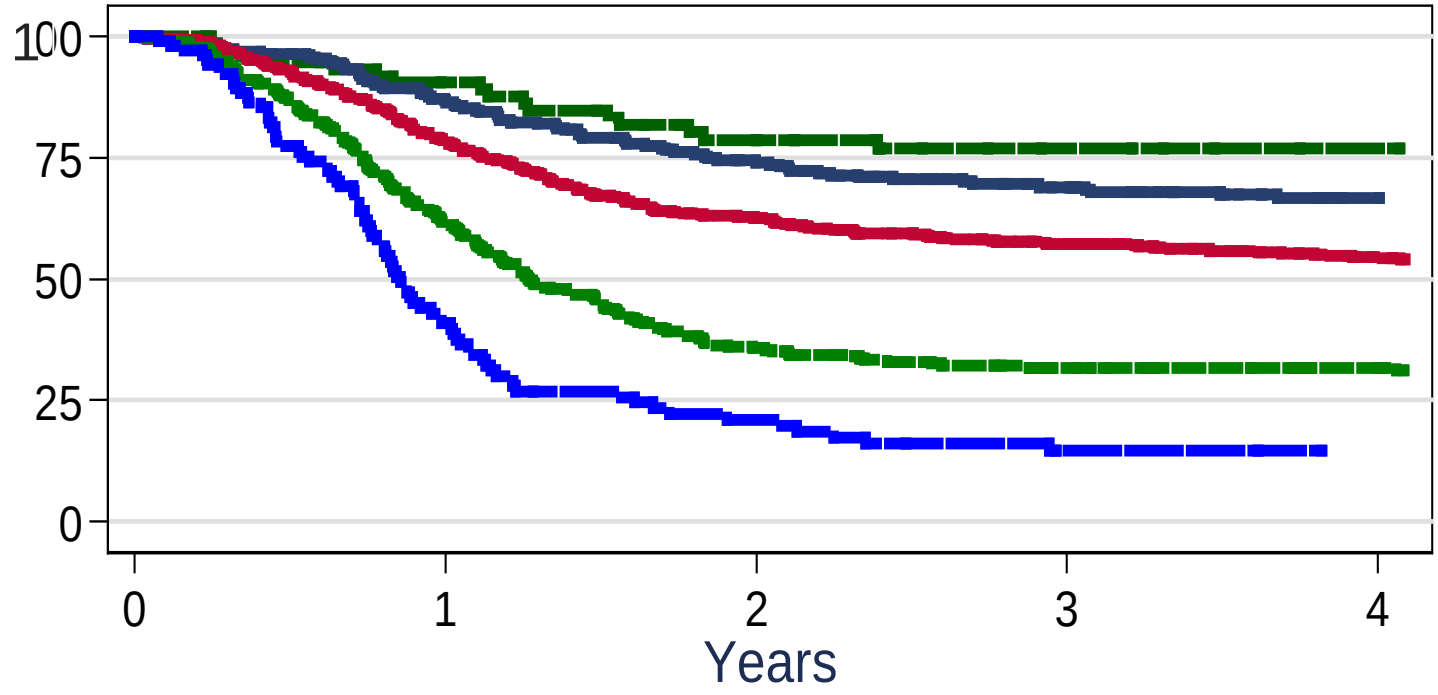
Overall Survival

All patients



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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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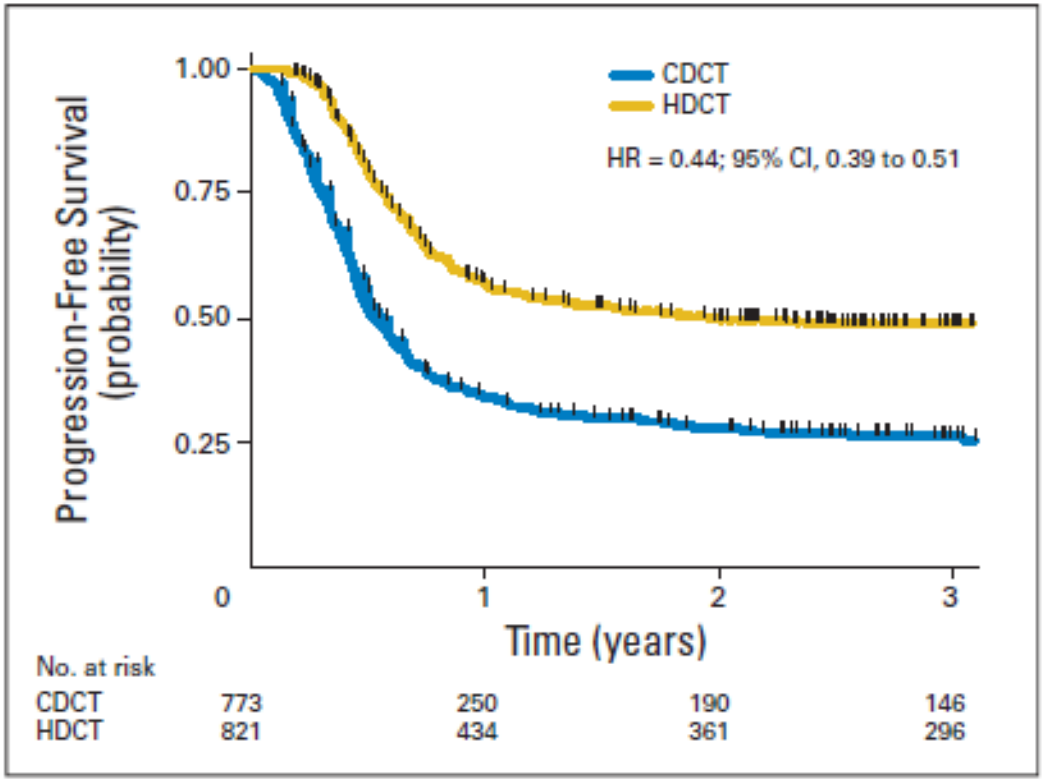

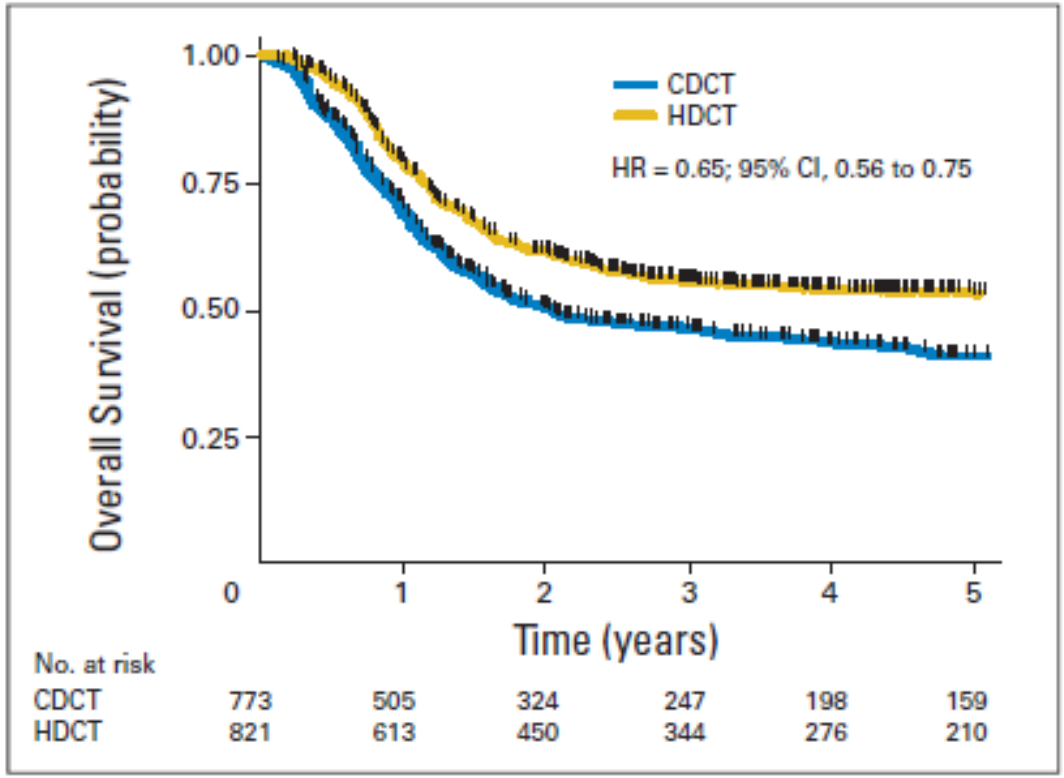

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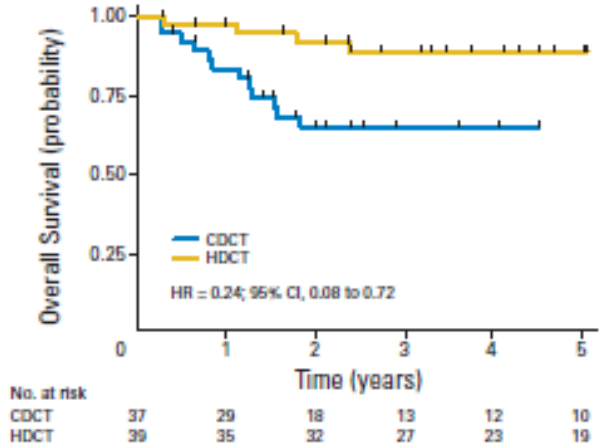
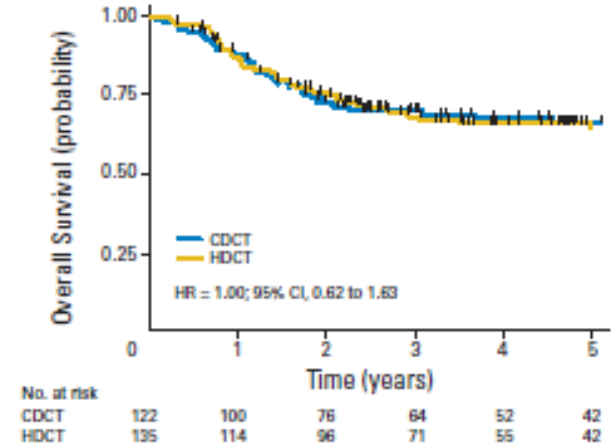
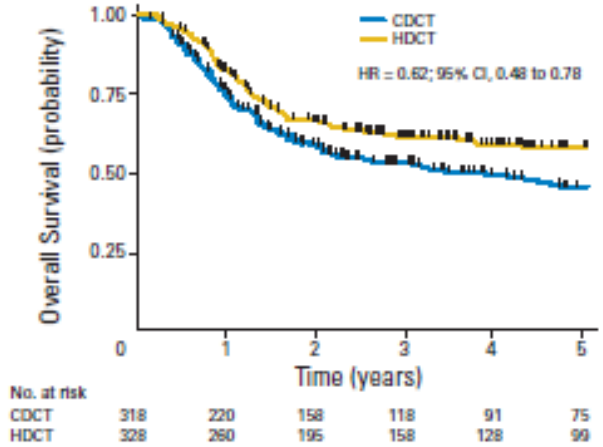
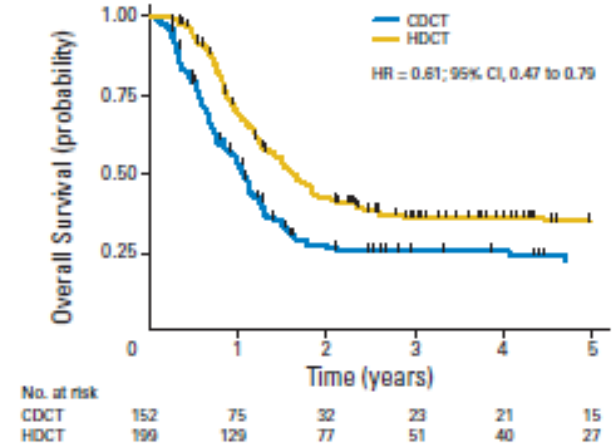
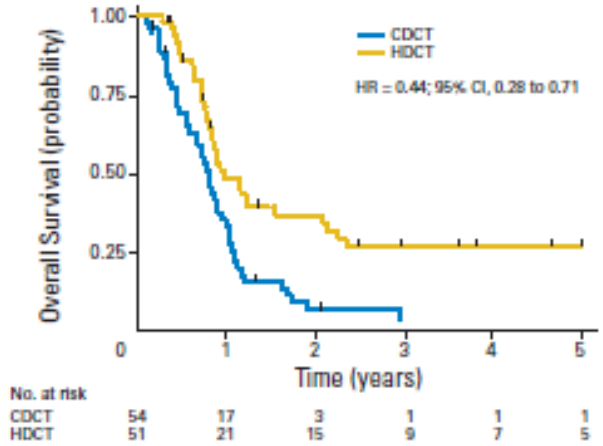




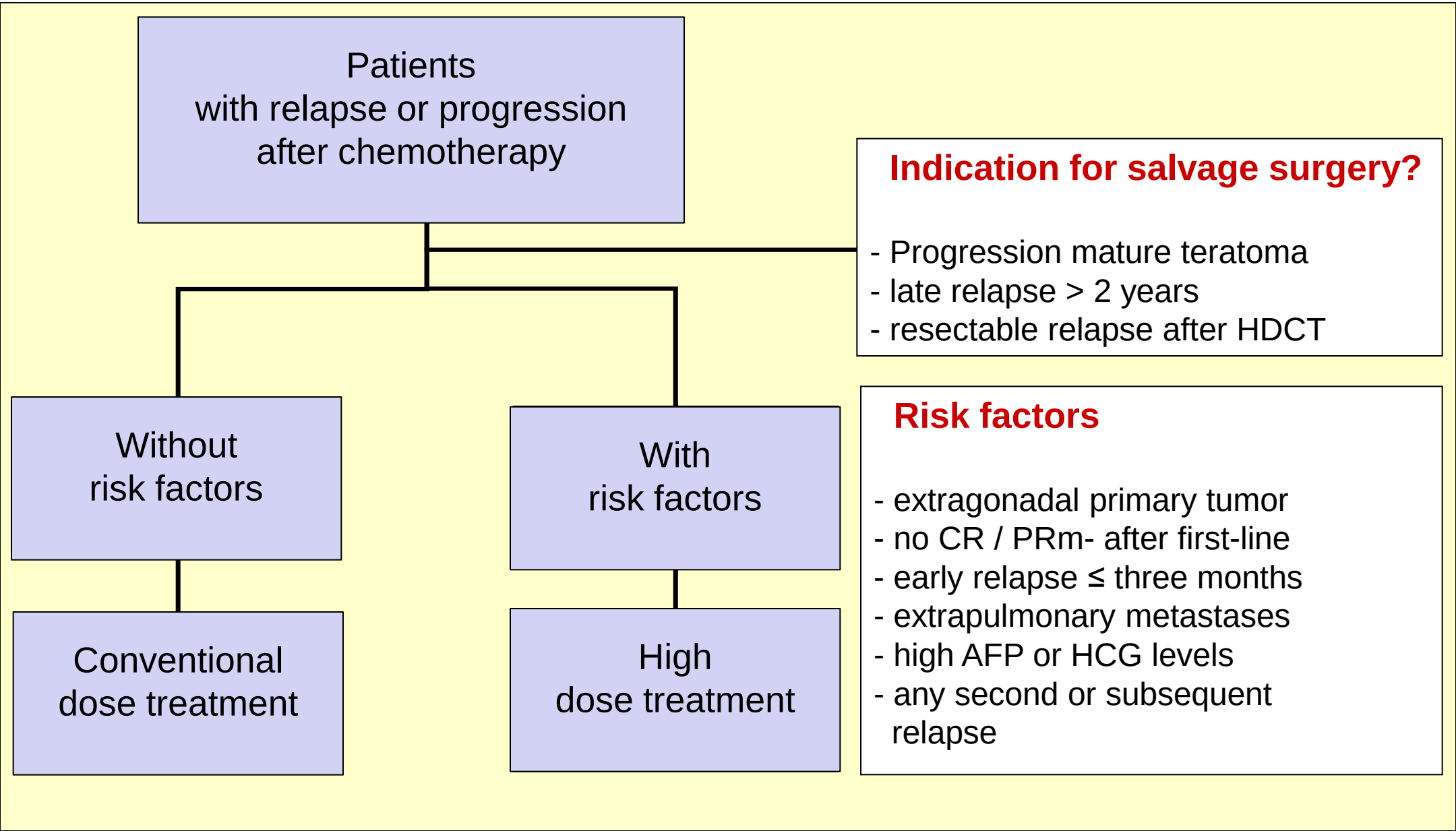




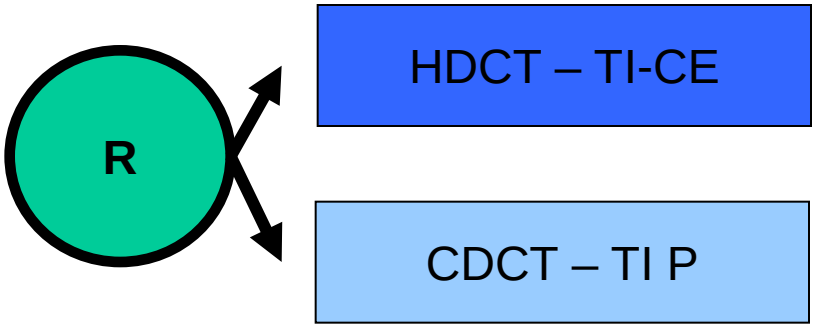


Overall survival according to risk categories

One possible strategy for first-salvage



TIGER study summary



HDCT=high dose chemotherapy
CDCT=conventional dose chemotherapy

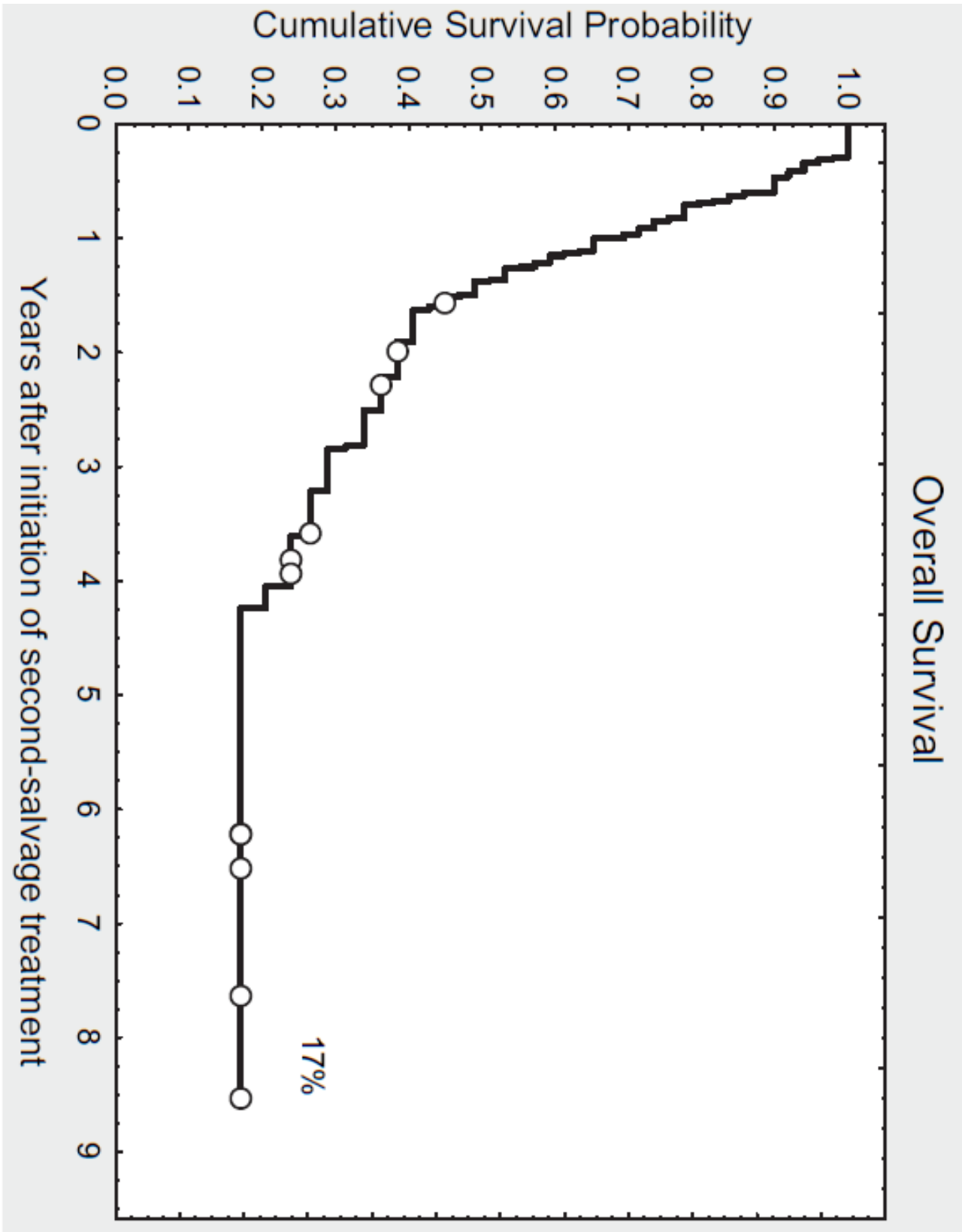
TI=paclitaxel ifosamide
C=cisplatin
CE=carboplatin and etoposide (high dose)

Eligibility	Primary endpoint	Number of patient	Duration of enrolment	Stratification
Relapsed GCT No previous taxane therapy	Overall survival	420	4 years	Risk score Country

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*]



Zusammenfassung

- In der Primärtherapie gibt es derzeit drei Gruppen die möglicherweise von einer Therapieintensivierung profitieren könnten
- Optimale Weg der Therapieintensivierung ist in der Primärtherapie ist unklar
- In der Salvagetherapie profitieren wahrscheinlich vor allem Patienten mit Risikofaktoren

http://www.hodenkrebs.de