

# Management of Testicular Seminomas



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# Surgery is always first

- Radical orchiectomy
- The tumour-bearing testis is resected with the spermatic cord at the level of the internal inguinal ring)
- Any scrotal violation for biopsy or open surgery should be avoided
- Tumour marker analysis should be carried out
  - Before
  - After surgery until normalisation
  - Progression
  - Plateau development
- Consider sperm banking (atrophic contralateral testis, planed for RT chemo, history of infertility)

# Management of opposite Testis

- 2%–5% contralateral TGCT chances (metachronously or synchronously)
- 3% and 5% of testicular cancer patients have TIN in the contralateral testis
- Highest risk (~30%) in men with testicular atrophy (volume <12 ml) and age <40 years, and in patients with EGGCT

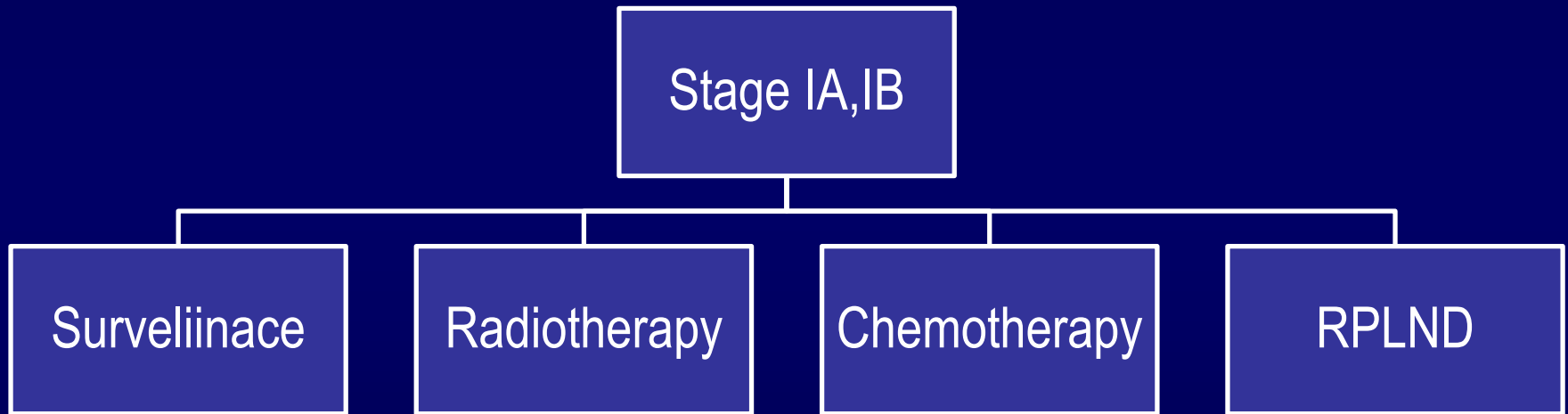
# Management of opposite Testis

- Routine biopsy of the contralateral testis is not indicated
- If a biopsy is carried out and TIN is diagnosed, however, the condition may be managed by
  - Surveillance
  - 20 Gy /10 # (with potential damage to the contralateral, nonaffected testis by scattered radiation)
  - Orchiectomy depending on fertility issues.
- In patients with metastatic disease treated with three or more cycles of cisplatin-based chemotherapy, TIN in the contralateral non-resected testicle may be eradicated or progression may be slowed down, although the risk of developing an invasive tumour is still substantial

# Risk stratification after orchidectomy IGCCCG

<b>Risk Status</b>	<b>Seminoma</b>
<b>Good Risk</b>	Any primary site and No nonpulmonary visceral metastases and Normal AFP Any hCG Any LDH
<b>Intermediate Risk</b>	Any primary site and Nonpulmonary visceral metastases and Normal AFP Any hCG Any LDH
<b>Poor Risk</b>	No patients classified as poor prognosis

# Stage IA , IB



# Surveillance

Series	No. Pts	Median FU (mo)	Relapse: No. Pts (%)	CSS (%)
Daugaard	394	60	69 (17.5)	100.0
Germa Lluch	233	33	38 (16)	100.0
Horwich	103	62	17 (16.5)	100.0
Oliver	67	61	16 (24)	97.0
Von der Maase	261	48	49 (18.8)	98.9
Tyldesley	93	33	16 (17.2)	97.8
Leung	484	79	72 (15)	99.8

- Relapse rates 14 - 19%
- The predominant site of relapse - paraaortic lymph nodes (93% in the Danish Testicular Cancer Study Group study and 84% in the PMH series)
- The median time to relapse ranged from 12 to 18 months

# RT

Author	Study Years	No. Pts	Relapse (%)	CSS (%)
Bayens	1975–1985	132	4.5	99.0
Coleman	1980–1995	144	4.2	100.0
Fossa	1989–1993	242	3.7	100.0
Hallemeier	1972–2009	199	2	99.0
Hultenschmidt	1978–1992	188	1.0	100.0
Santoni	1970–1999	487	4.3	99.4
Warde	1981–1989	282	5.0	100.0

- Relapse rates 0.5 - 5%
- The most common sites of relapse following adjuvant RT are the mediastinum, lungs, and left supraclavicular fossa
- Frequently occurs within the first 2 to 3 years



# Chemotherapy

Author	Study Years	ARM		Relapse (%)	CSS (%)
MRC TE19/EORTC 30982	1996–2001	1 cycle Carboplatin	573	5.3	100
		RT	905	4	100
Klaus-Peter Dieckmann –	2009-2015	1 cycle Carboplatin	66	1.5	100
		2 cycle Carboplatin	362	5	100

- Relapse rates 1.5 - 5%
- Relapsed more frequently in the PA nodes

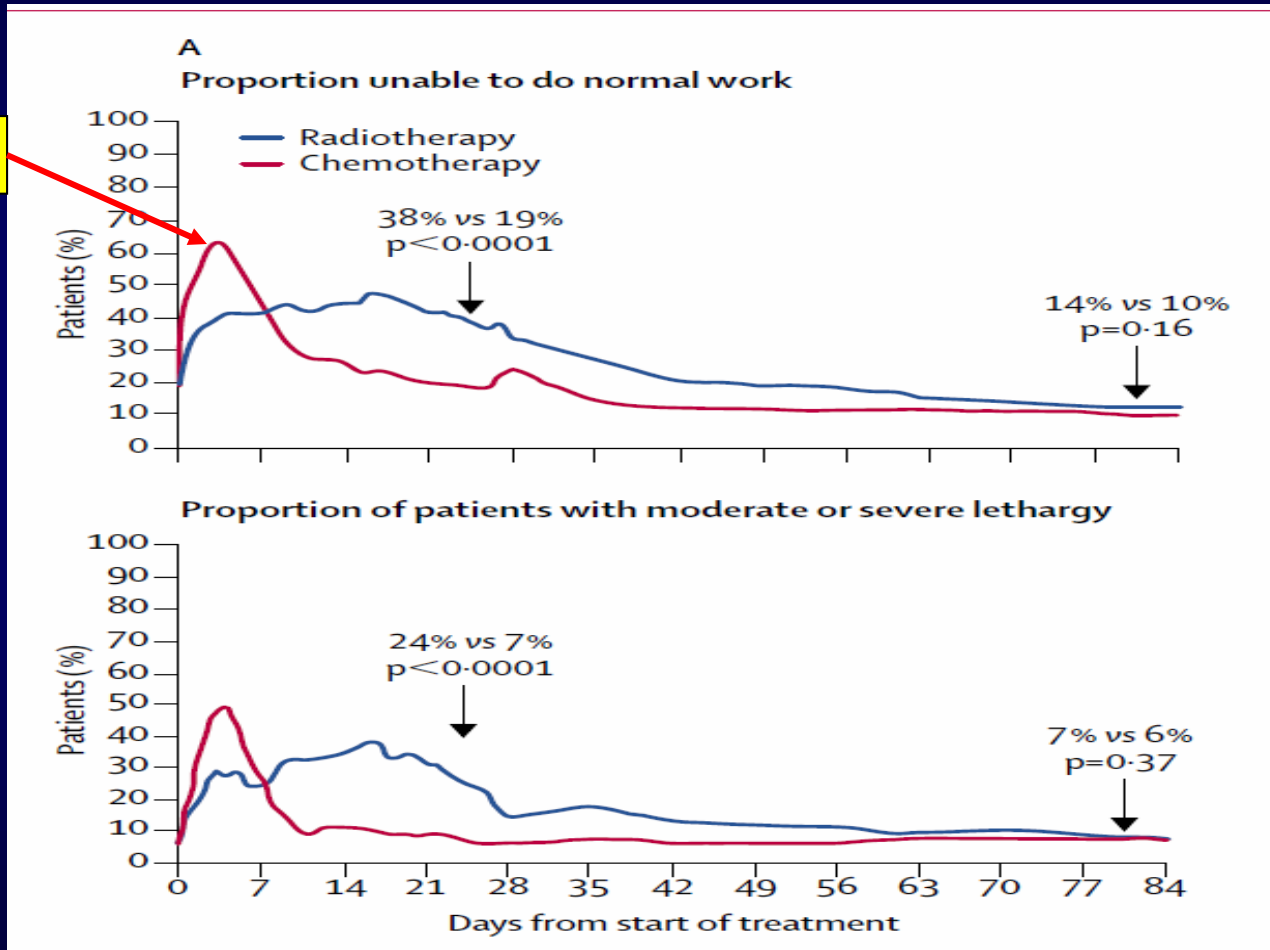
# Chemo 1 cycle vs 2 cycle

Author	Intervention	No. Pts	Relapse (%)	CSS (%)
Klaus-Peter Dieckmann – 2009-2015	Surveillance	573	8.2	100
	Radiotherapy 20Gy	41	2.4	100
	1 cycle Carboplatin	362	5	100
	2 cycle Carboplatin	66	1.5	100

**p = 0.0573**

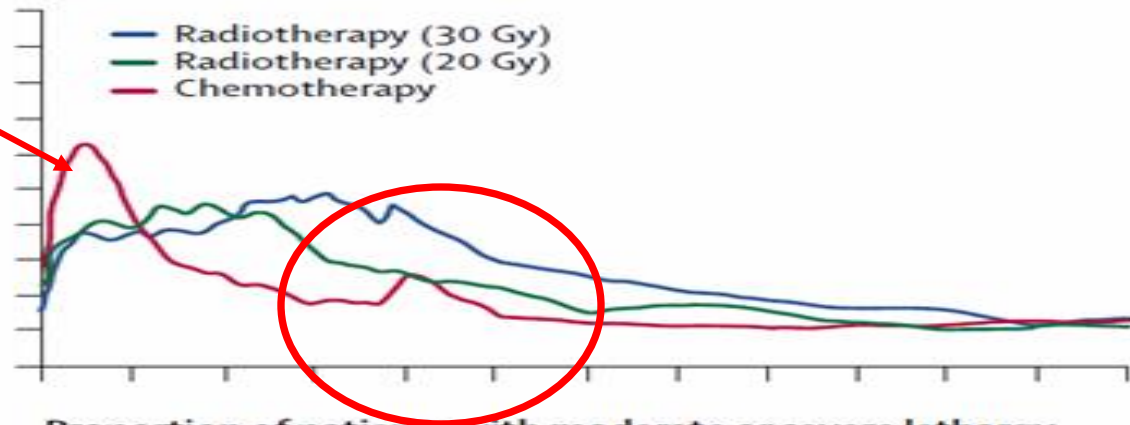
# RT vs Chemo

Initial 72 hrs

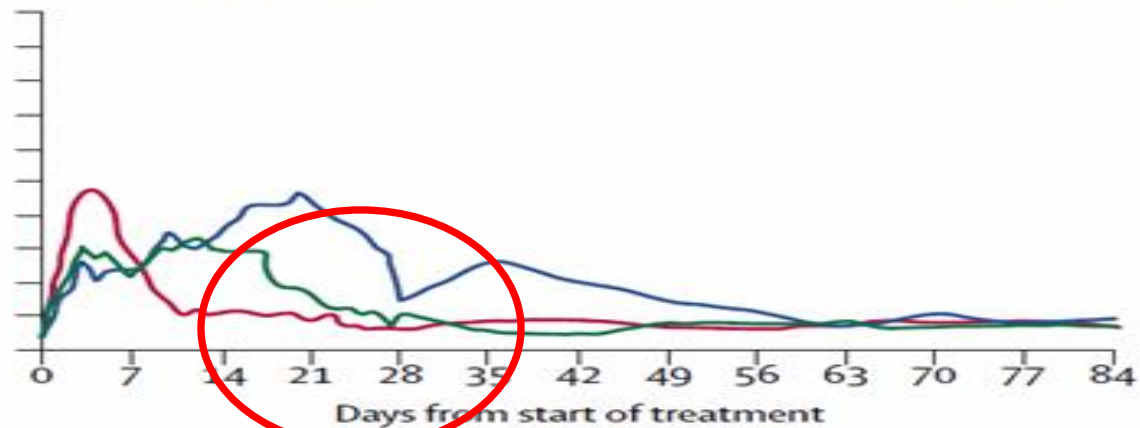


# RT vs Chemo

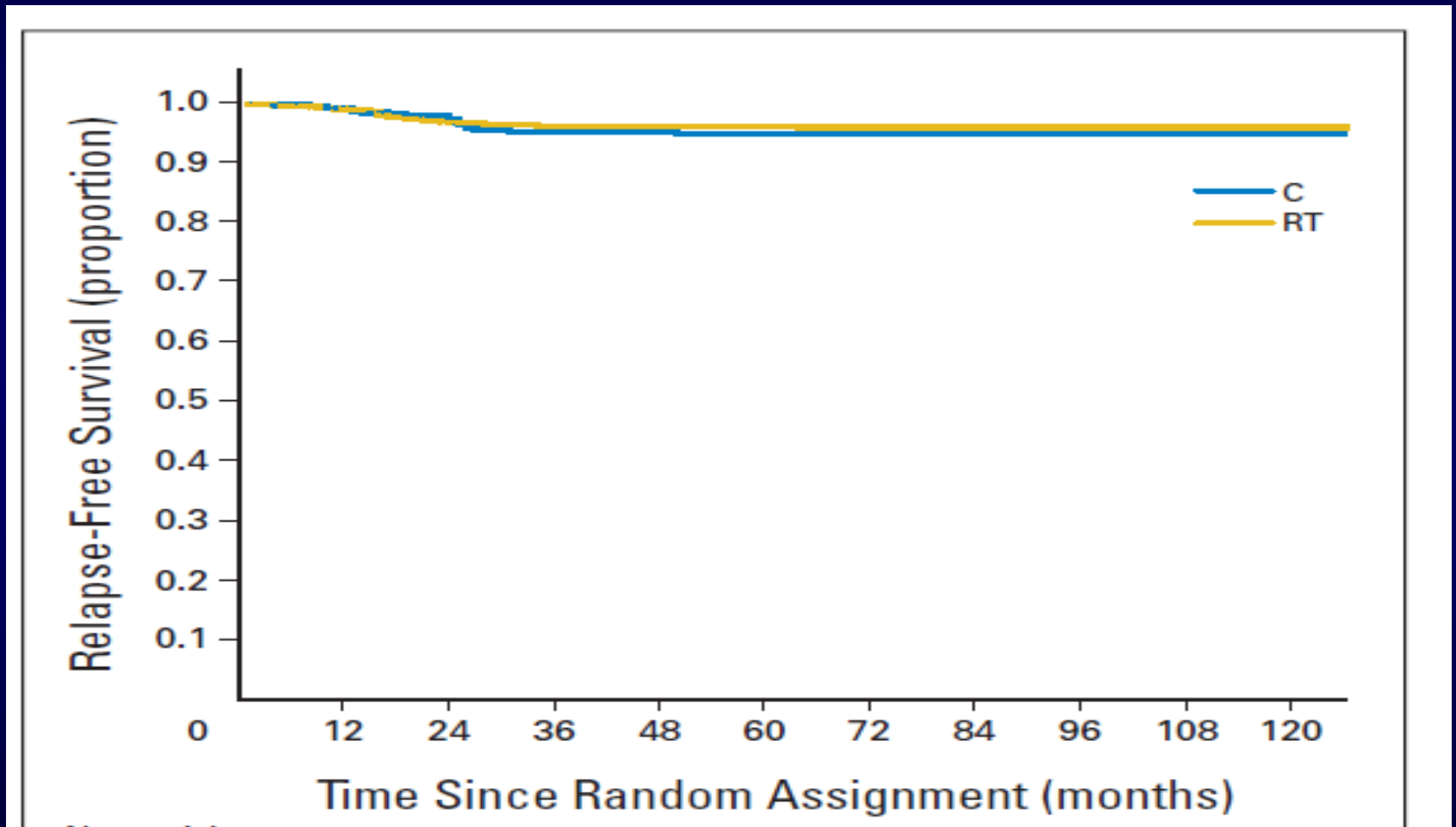
B  
Proportion unable to do normal work



Proportion of patients with moderate or severe lethargy



# RT vs Chemo



# RT vs Chemo

**Table 1.** Summary of Events

Event	Treatment Arm			
	Carboplatin (n = 573)		Radiotherapy (n = 904)	
	No.	%	No.	%
Total relapse	29	5.1	37	4.1
New primary cancers	7	1.2	25	2.8
GCT	2		15	
Other	5		10	
Total deaths	6	1.0	10	1.1
Death as a result of seminoma	0		1	
Death as a result of other cause	6		9	

Abbreviation: GCT, germ cell tumor.

# Timor Size and Rete Testis Invasion

Author	Intervention	No. Pts	Relapse (%)	5 yr CSS (%)
Padraig Warde et al median follow up 7 yrs	<b>Surveillance</b>	638 From 4 institute	<b>82.3</b>	99.3

**Table 2. Candidate Prognostic Factors: Univariate Analysis**

Variable	No.	5-Year Relapse-Free Rate (% $\pm$ SE)	P (likelihood $\chi^2$ )
<b>Tumor size</b>			
$\leq 4$ cm	317	86.6 $\pm$ 2.0	.003
$> 4$ cm	281	75.9 $\pm$ 2.6	
<b>Age</b>			
$\leq 36$ years	344	83.2 $\pm$ 2.1	.68
$> 36$ years	292	81.2 $\pm$ 2.3	
<b>Small vessel invasion</b>			
Absent	384	85.6 $\pm$ 1.8	.038
Present	191	77.3 $\pm$ 3.1	
<b>Histologic features</b>			
Classical	548	83.2 $\pm$ 1.6	.056
Anaplastic	50	71.4 $\pm$ 6.5	
<b>Rete testis invasion</b>			
Absent	299	86.3 $\pm$ 2.0	.003
Present	176	76.7 $\pm$ 3.3	

# Surveillance vs Chemo

(risk factor tumor size and rete testis invasion)

Author	Intervention	No. Pts	Relapse Rate (%)	Relapse (%) Without risk factor	Relapse (%) With one or two risk factor	5 yr CSS (%)
T. Tandstad (SEWNOTECA) 2007-2010	Surveillance	469	7.5	4	15.5 (p<0.001)	100
	One cycle carboplatin	422	6.2	2.2	9.3 (p=0.001)	100

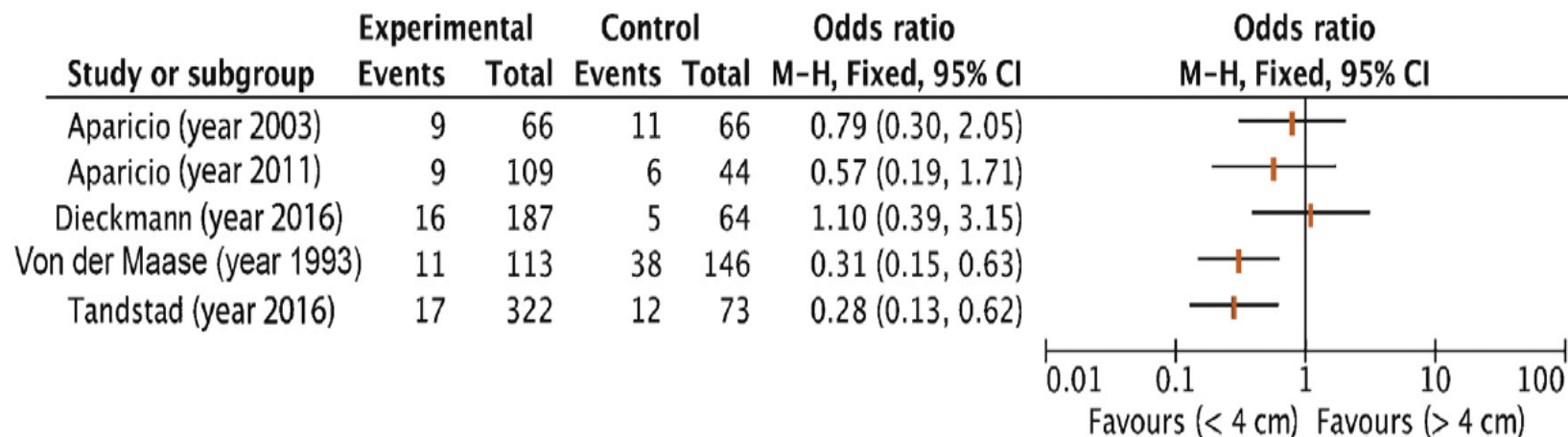
Factor	Univariable analysis				Multivariable analysis <sup>b</sup>		
	N of patients	HR	95% CI		N of patients	HR	95% CI
Tumor size							
≤4 cm	696 (63%)	1.0			635	1.0	
>4 cm	414 (37%)	3.1	1.8–5.1	<i>P</i> < 0.001	362	2.7	1.6–4.6
Missing	2						
Invasion rete testis							
Absent	726 (65%)	1.0			726	1.0	
Present	273 (25%)	2.2	1.4–3.7	<i>P</i> = 0.001	271	1.9	1.2–3.2
Missing	113 (10%)						

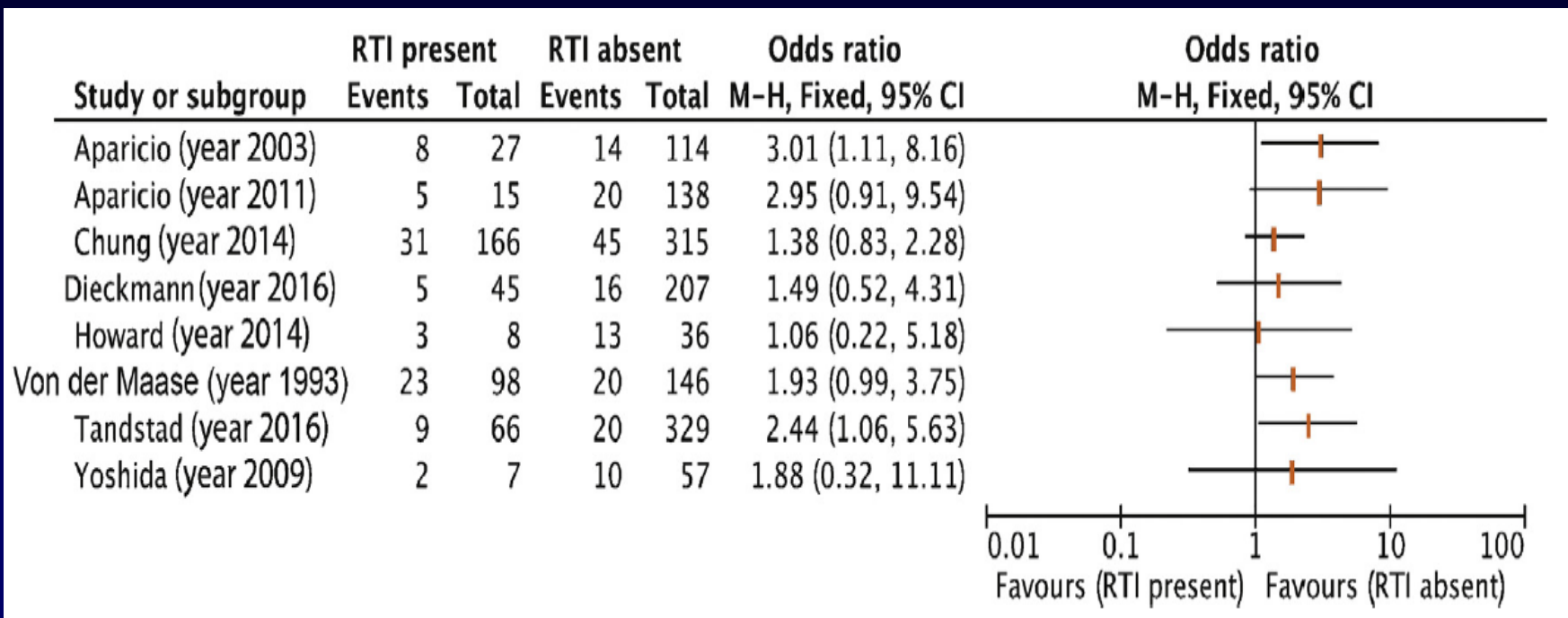


## Review – Testis Cancer

# Testicular Tumour Size and Rete Testis Invasion as Prognostic Factors for the Risk of Relapse of Clinical Stage I Seminoma Testis Patients Under Surveillance: a Systematic Review by the Testicular Cancer Guidelines Panel

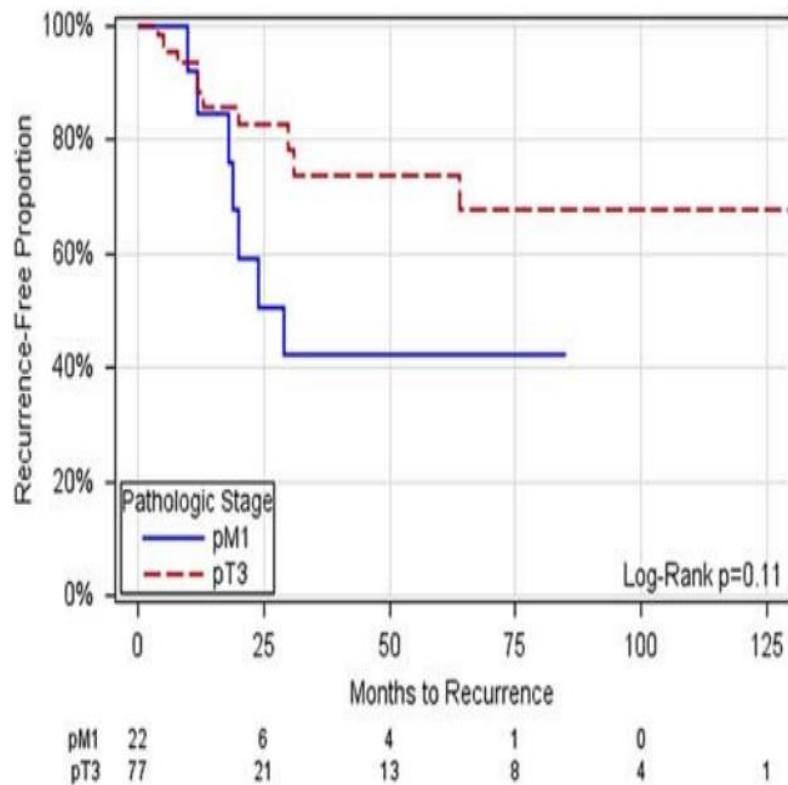
Joost L. Boormans<sup>a,†,\*</sup>, Javier Mayor de Castro<sup>b,†</sup>, Lorenzo Marconi<sup>c</sup>, Yuhong Yuan<sup>d</sup>,  
M. Pihl<sup>e</sup>, L. B. de Groot<sup>f</sup>, R. L. F. Niels<sup>g</sup>, F. M. J. de Boer<sup>h</sup>, J. L. H. de Boer<sup>i</sup>



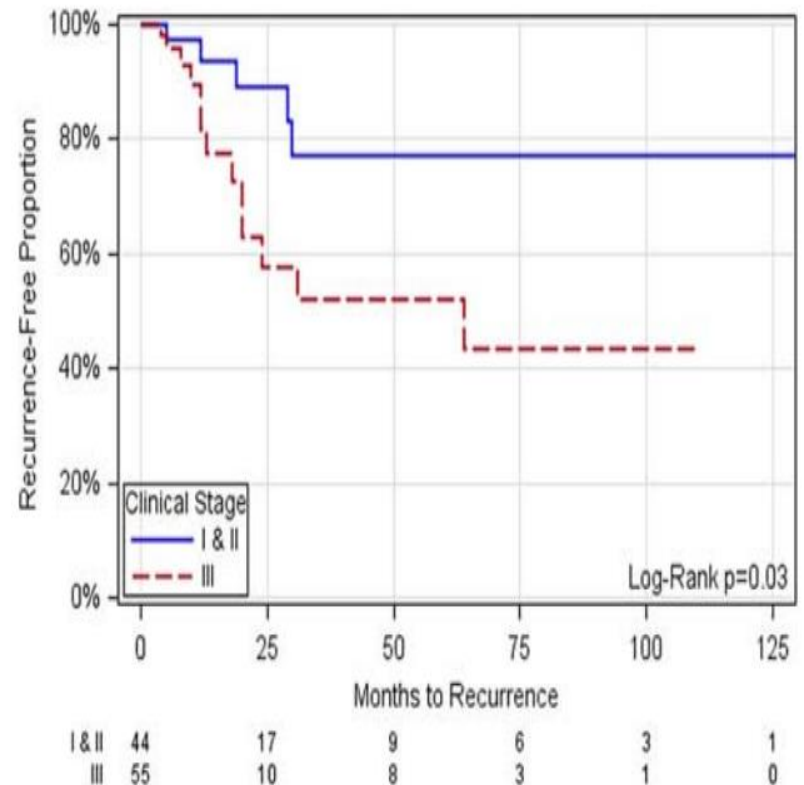


**Patient summary:** Primary testicular tumour size and rete testis invasion are considered to be important prognostic factors for the risk of relapse in patients with clinical stage I seminoma testis. We systematically reviewed all the literature on the prognostic value of these two postulated risk factors. The outcome is that the prognostic power of these factors in the published literature is too low to advocate their routine use in clinical practice and to drive the choice on adjuvant treatment in clinical stage I seminoma testis patients.

# Spermatic cord issue



**FIGURE 2.** Kaplan-Meier curve of time to recurrence by pathologic stage.



**FIGURE 4.** Kaplan-Meier curve of time to recurrence by combined CSI and CSII vs. CSIII.

# Spermatic cord issue

- New AJCC - discontinuous spermatic cord involvement as pM1
- NCCN - To be considered as pT3 (high Risk – treat accordingly)
- If surveillance – then recurrence mostly in pelvis so include imaging

**TABLE 4.** Patients With Known Recurrence of GCT

	Total	Recurrence (n [%])	<i>P</i>
Pathologic stage			0.12
pT3	77	12 (15.6)	
pM1	22	7 (31.8)	
CS			0.48
I	7	1 (14.3)	
II	37	5 (13.5)	
III	55	13 (23.6)	

# Surveillance vs RT vs Chemo

	Radiation (n=329)	Chemotherapy (n=79)	Observation (n=94)	P
Median age (y)	36	32	38	0.066
T stage (%)	T1: 76.6 T2: 20.4 T3: 2.7 T4: 0.3	T1: 63.3 T2: 31.6 T3: 3.8 T4: 1.3	T1: 76.6 T2: 20.2 T3: 1.1 T4: 1.1 Unknown: 1.1	0.222
Median tumor size (cm)	4.0	4.3	3.8	0.455
LVI present (%)	24.0	38.0	20.2	0.016
Rete testis invasion present (%)	17.6	20.3	17.0	0.834
Epididymis invasion present (%)	4.6	6.3	3.2	0.616
Invasion through tunica albuginea present (%)	4.3	6.3	3.2	0.593
Preoperative hCG elevated (%)	14.3	31.6	20.2	0.001
Preoperative LDH elevated (%)	22.8	29.1	25.5	0.437

- N – 502
- 1990 -2010

# Surveillance vs RT vs Chemo

**TABLE 3. Outcome by Management Strategy**

	<b>Radiation</b>	<b>Chemotherapy</b>	<b>Observation</b>
Relapse-free survival (y)			
2	97.6% (95.8, 99.4)	98.3% (94.9, 100)	89.2% (81.4, 95.4)
5	97.2% (95.2, 99.1)	—	89.2% (81.4, 95.4)
Overall survival (y)			
2	99.6% (97.7, 100)	100% (100, 100)	98.8% (96.2, 100)
5	98.0% (95.2, 99.3)	—	98.8% (96.2, 100)
Cause-specific survival (y)			
2	99.6% (98.2, 100)	100% (100, 100)	100% (100, 100)
5	99.3% (98.2, 100)	—	100% (100, 100)

**RFS lower in observation group**

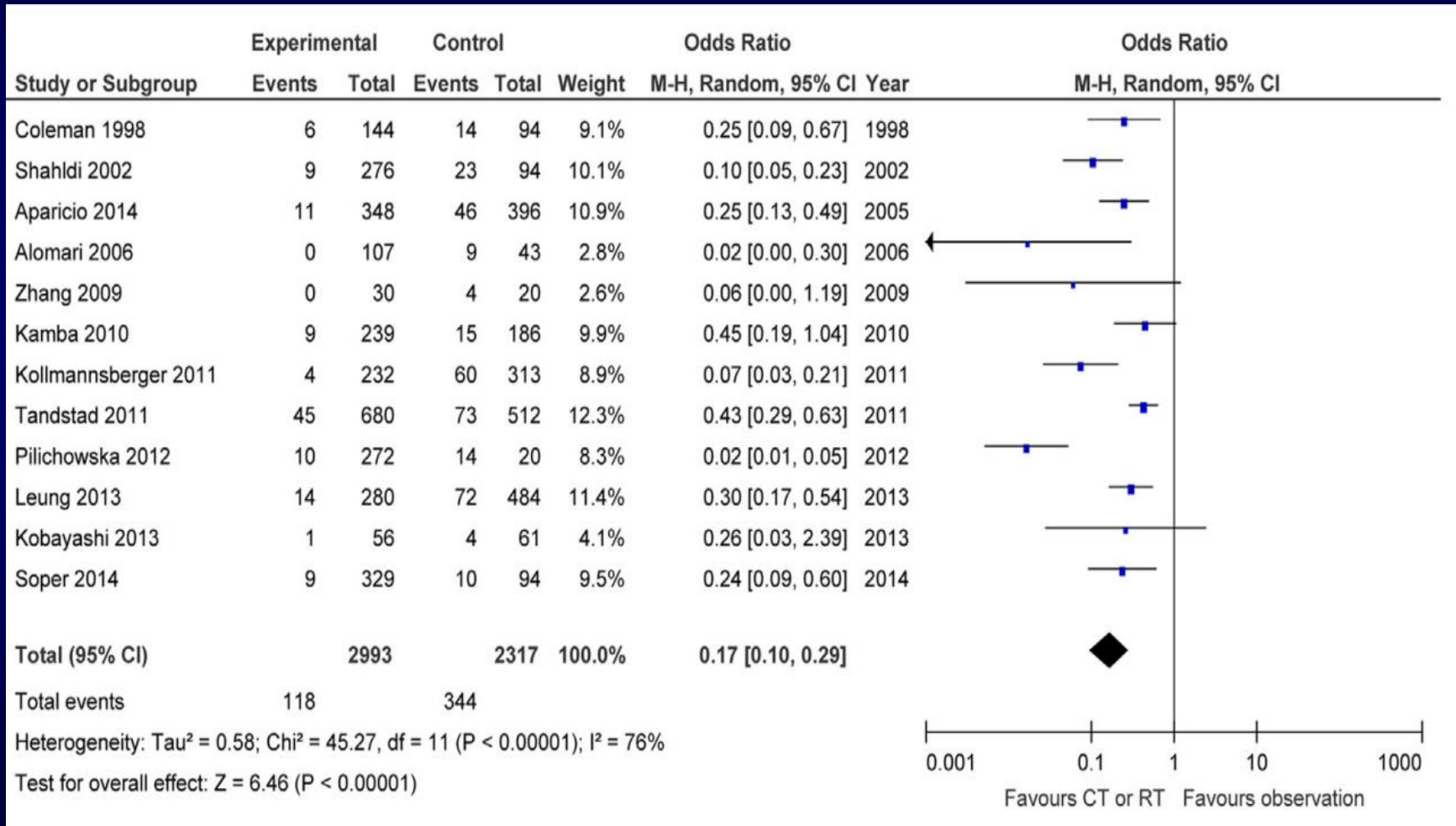
**Overall Survival is similar observation group**

# RPLND

- Only for patients refuse surveillance / RT or Chemo (Inflammatory bowel disease)
- Generally not done nowadays

# 5 yr RFS

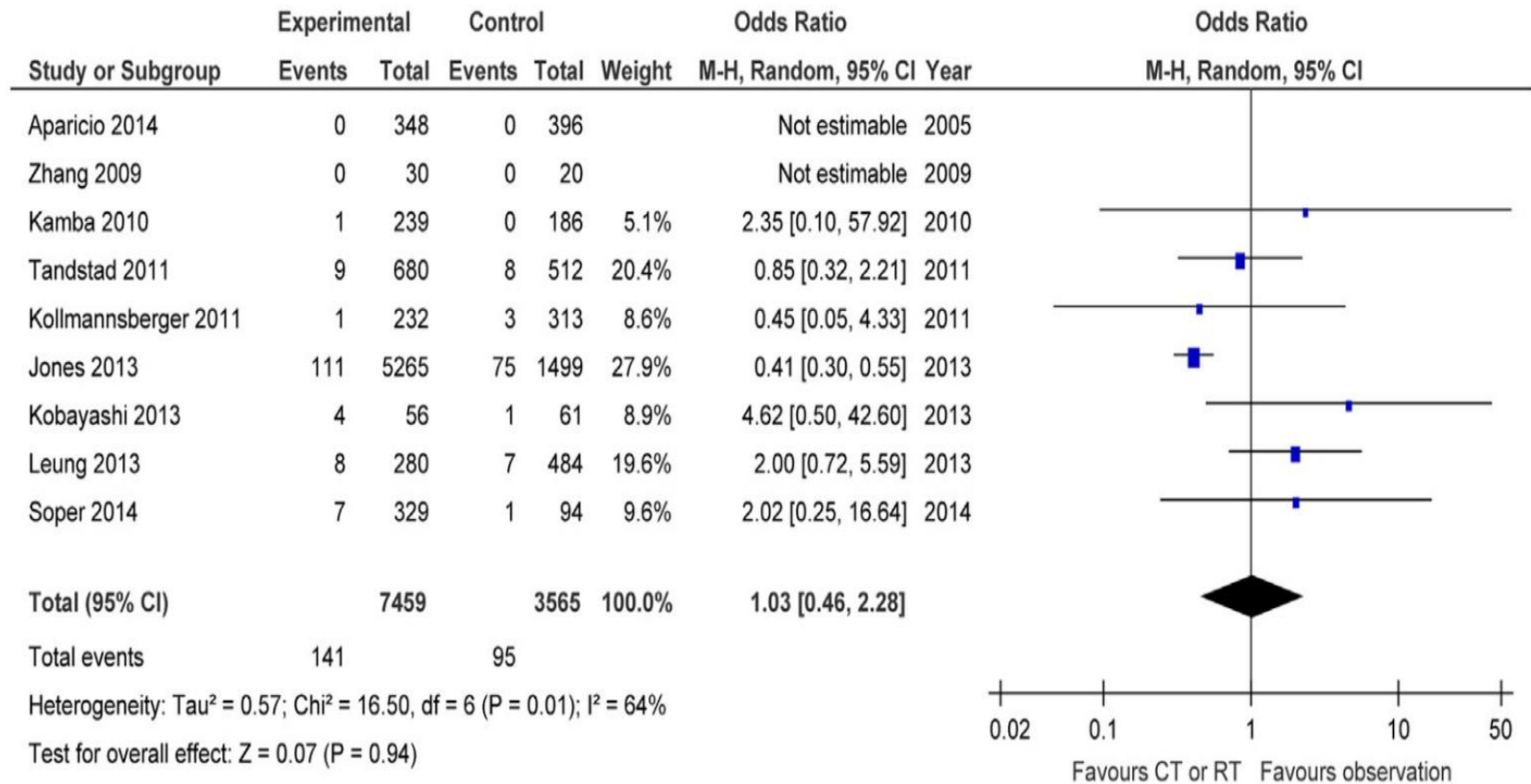
## 13 trials N=12075





# 5 ys OS

## 13 trials N=12075

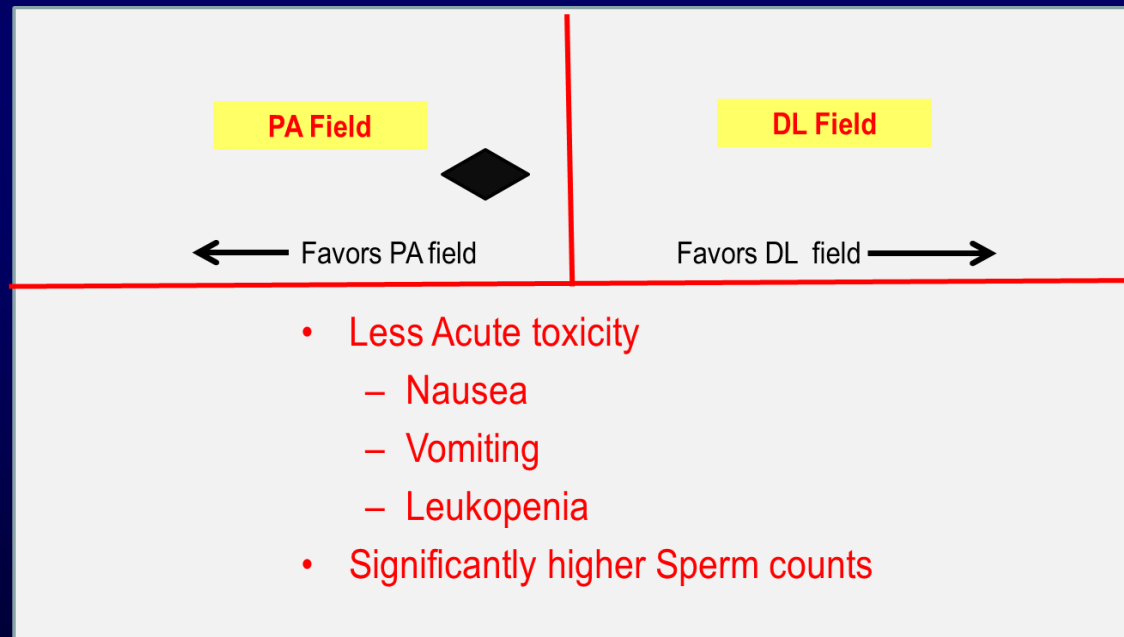


# Para aortic (PA – Strip) or Dog Leg/Hockey Stick (DL-field)

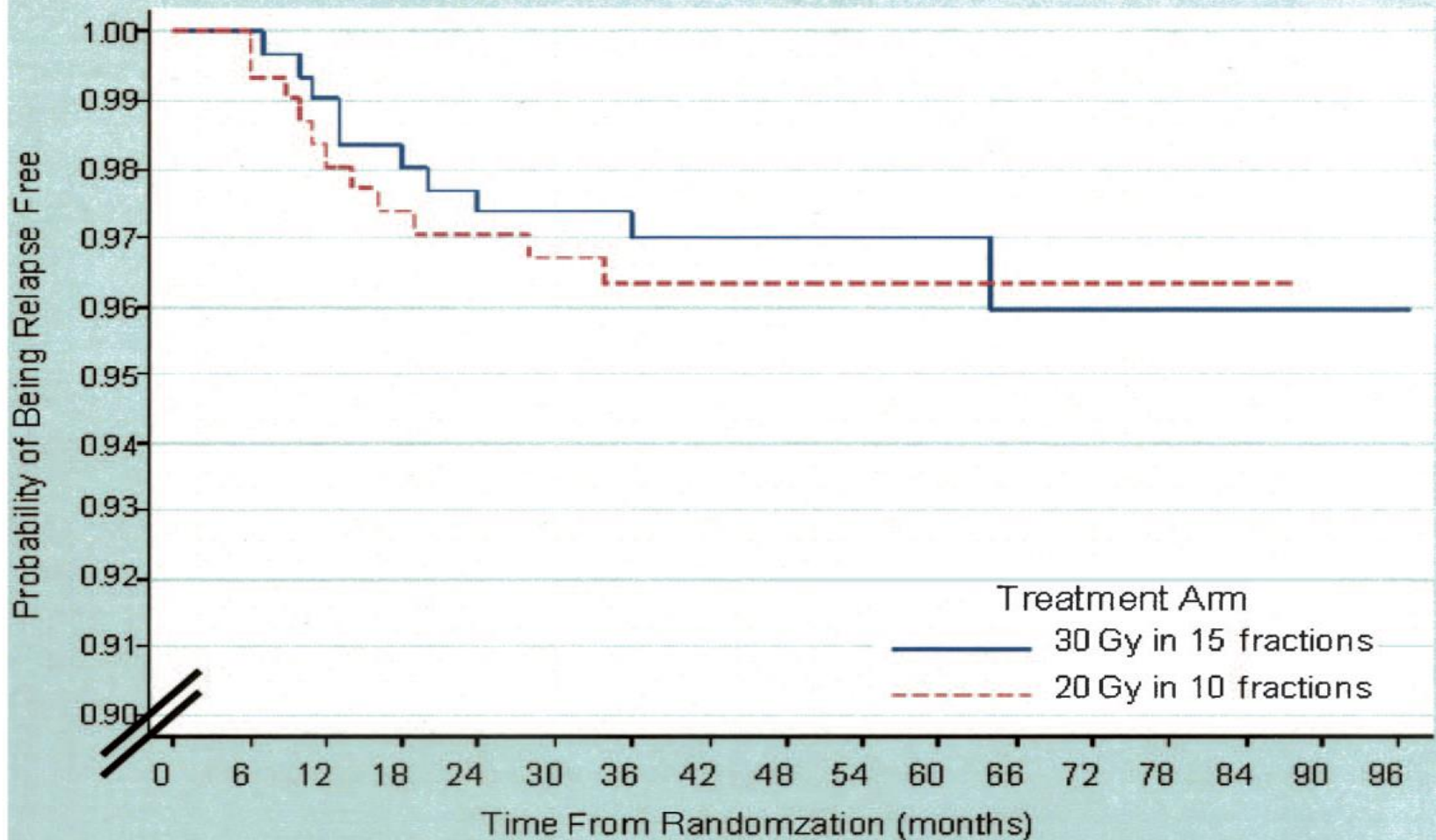
Author	No. Pts	Relapse Abdomen	Relapse Pelvis
H von der Maase 1985-1988	261	83	2
Torgrim Tandstad 2000-2006	1192	94	

# Para aortic (PA – Strip) or Dog Leg (DL-field) MRC TE 10

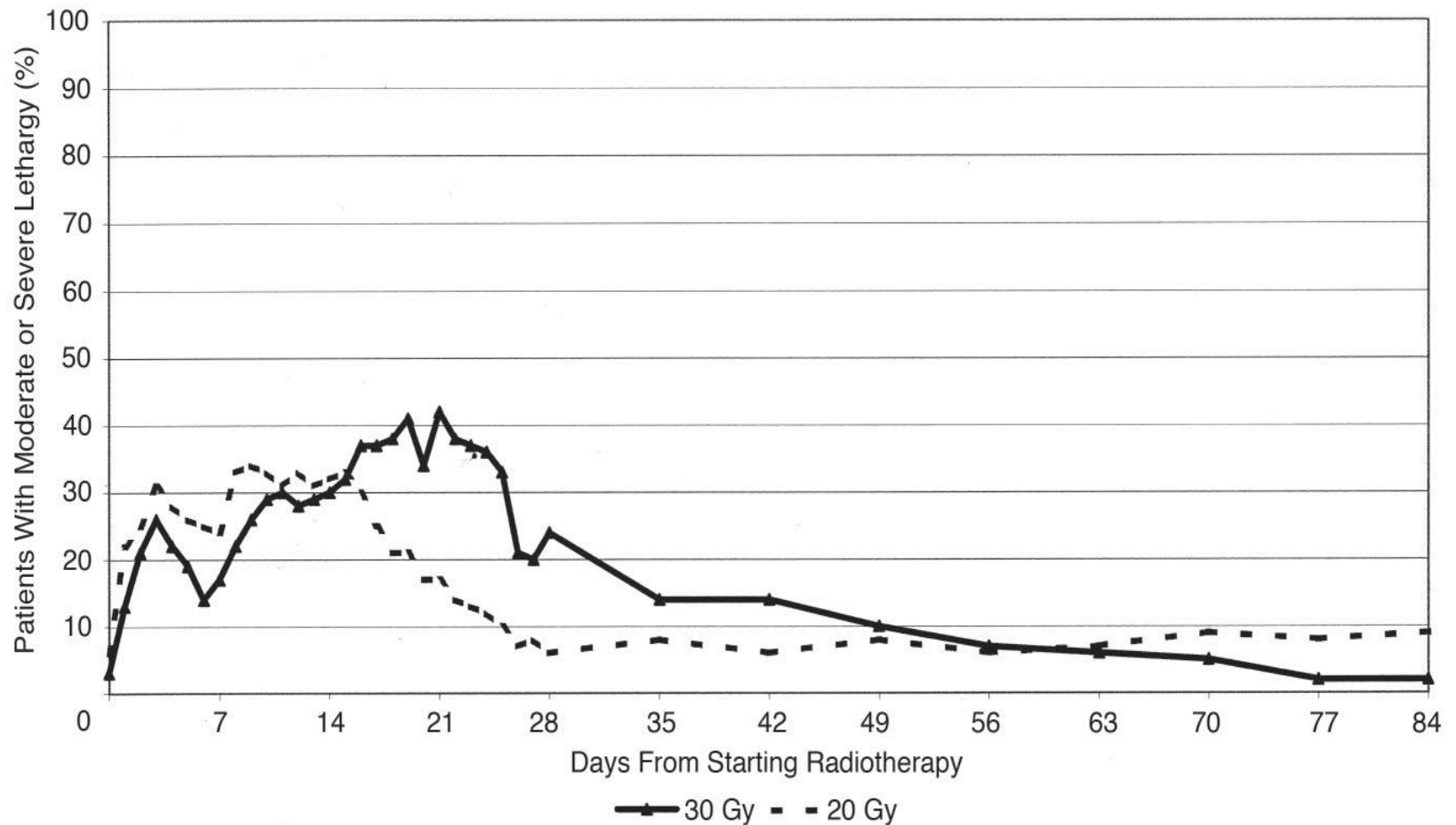
Author	Intervention	No. Pts	3 yr Relapse (%)	3 yr CSS (%)
Fossa et al 1989-1993	PA field	236	4	99.3
	DL field	242	3.4	100



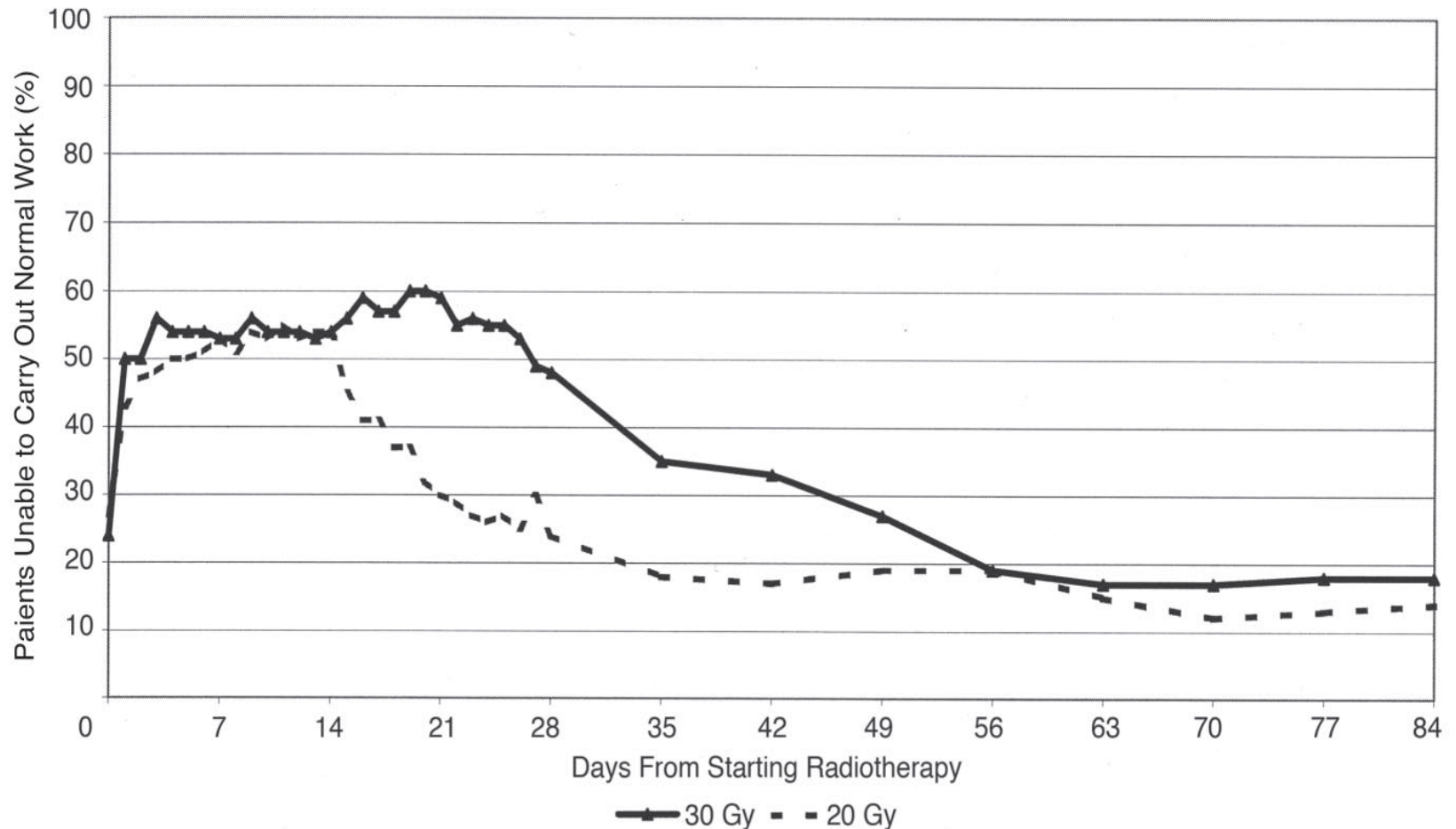
# 30 Gy vs 20 Gy MRC TE 18



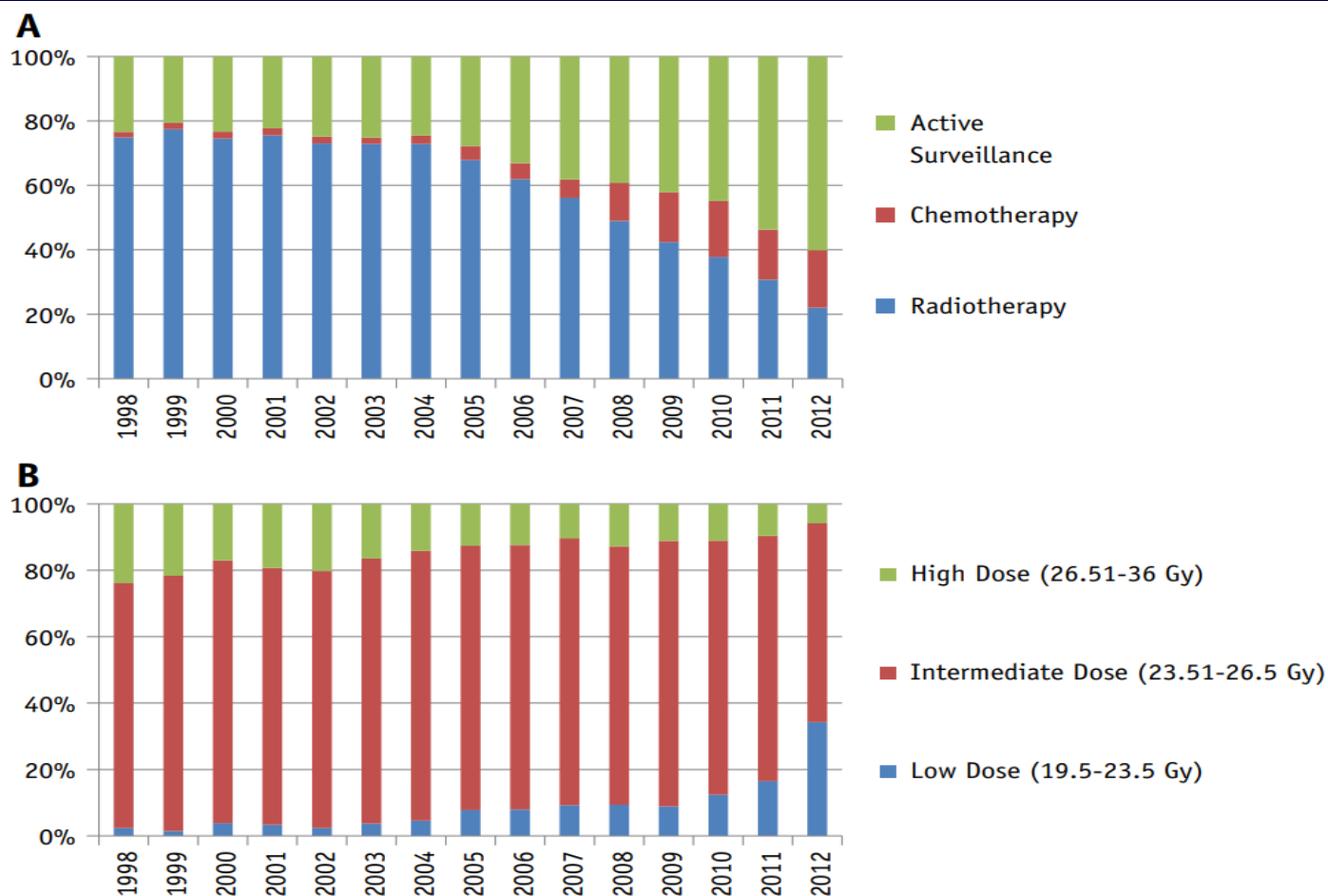
# Patient diary - Lethargy



# Patient diary – return to normalcy



# Treatment trends US NCDB data 1998-2012 N=33094



**Fig. 1.** Trends in treatment selection over time. (A) Treatment modality, and (B) radiation therapy

## Stage IS

- Persistent elevation of tumour markers after orchiectomy
- Increased risk of disease outside retroperitoneum
- Systemic therapy is encouraged
- Repeat marker levels / CT scans



# Stage 1

- Stage I disease~ 80% of presentation
- Survival of ~99%, independent of the chosen strategy
- Minimising toxicity is the priority
- Surveillance is considered the preferred strategy
- The predictive value of 'risk factors', such as rete testis infiltration and tumour size  $\geq 4$  cm, is controversial
  - sometimes used to apply one course of carboplatin (AUC 7) or radiotherapy (20 Gy/10 # to para-aortic target volume) as adjuvant treatment
- Compared with radiotherapy, one course of carboplatin results in similar relapse rates, but less protracted treatment-related lethargy, sick leave and probably treatment-induced malignancies
- Relapse usually located in the retroperitoneal or iliac lymph nodes.
- Rarely, late occurring relapses may contain non-seminoma components

# Stage I seminoma – management

- Surveillance/RT/Chemotherapy all are equal options
- Relapse are also ~ 100% curable
- Risk factor Tumour Size >4cm or Rete Testis Invasion still not valid points to offer RT or Chemotherapy
- Although Observation has higher relapse rates they are salvaged with equal Overall Survival rates
- RT to PA field only with 20Gy/10# use of LA with conformal technique is advocated
- Carboplatin AUC 7 x 1 Cycle

# Stage IIA & IIB

- RT or Chemo (BEP x 3 or EP x 4)
- **No randomised data**

Author	Stage (N)	Intervention		5 yr OS (%)		
		RT	Chemotherapy	RT	Chemotherapy	P value
Glaser et al 1998- 2012 NCDB data	<b>IIA (960)</b>	<b>750</b>	<b>210</b>	<b>99</b>	<b>93</b>	<b>0.027</b>
	<b>IIB (812)</b>	<b>442</b>	<b>370</b>	<b>95.2</b>	<b>92.4</b>	<b>NS</b>

# Stage IIA & IIB

Author	Stage (N)	Intervention		5 yr OS (%)		
		RT	Chemotherapy	RT	Chemotherapy	P value
Paly et al 1998- 2012 NCDB data	IIA	1159	726	99.4	91.2	< 0.01
	IIB			96.1	92.8	P = 0.08

# BEP x 3 vs BEP x 4

Author	Randomisation	2yr PFS(%)	Toxicity
R de Wit et al. EORTC Good Prognosis GCT 1995-1998 Median follow up 2.1 yr	<b>BEP – 3 cycle</b>	90.4	Frequencies of hematologic and nonhematologic toxicities were essentially similar.
	<b>BEP – 4 cycle</b>	89.4 <b>P = 0.0075</b>	

# BEP x 3 vs EP x 4

Author	Randomisation	CR rates (%)	Relapse (%)	OS (%)	Acute toxicity
R de Wit et al. EORTC/GTCCG Good Prognosis NSGCT Follow up median 7.3yrs	<b>BEP - 200</b>	<b>95</b>	<b>4</b>	<b>Similar in both groups</b> <b>P = .262</b>	<b>More pulmonary and neurotoxicity , more Raynaud's phenomenon</b>
	<b>EP – 195</b> (Lower dose of etoposide 360mg/m2)	<b>87</b> <b>P = 0.0075</b>	<b>4</b> <b>NS</b>		
S Culine et al. GETUG T93BP) Good Prognosis NSGCT Follow up median 4.4 yrs	<b>BEP – 131</b>	<b>82</b>	<b>7</b>	<b>97</b>	
	<b>EP– 126</b>	<b>75</b> <b>NS</b>	<b>14</b> <b>P=0.052</b>	<b>93</b> <b>P=0.082</b>	

R de Wit et al. JCO 1997  
S Culine et al. Ann Oncol 2007

# EP x 4

Author	Randomisation	CR rates (%)	Relapse (%)	OS (%)
G. Varuni Kondagunta,et al Good Prognosis NSGCT and seminoma Median follow up 7.7 yrs	Seminoma - 80 non seminoma - 209	98	6	94

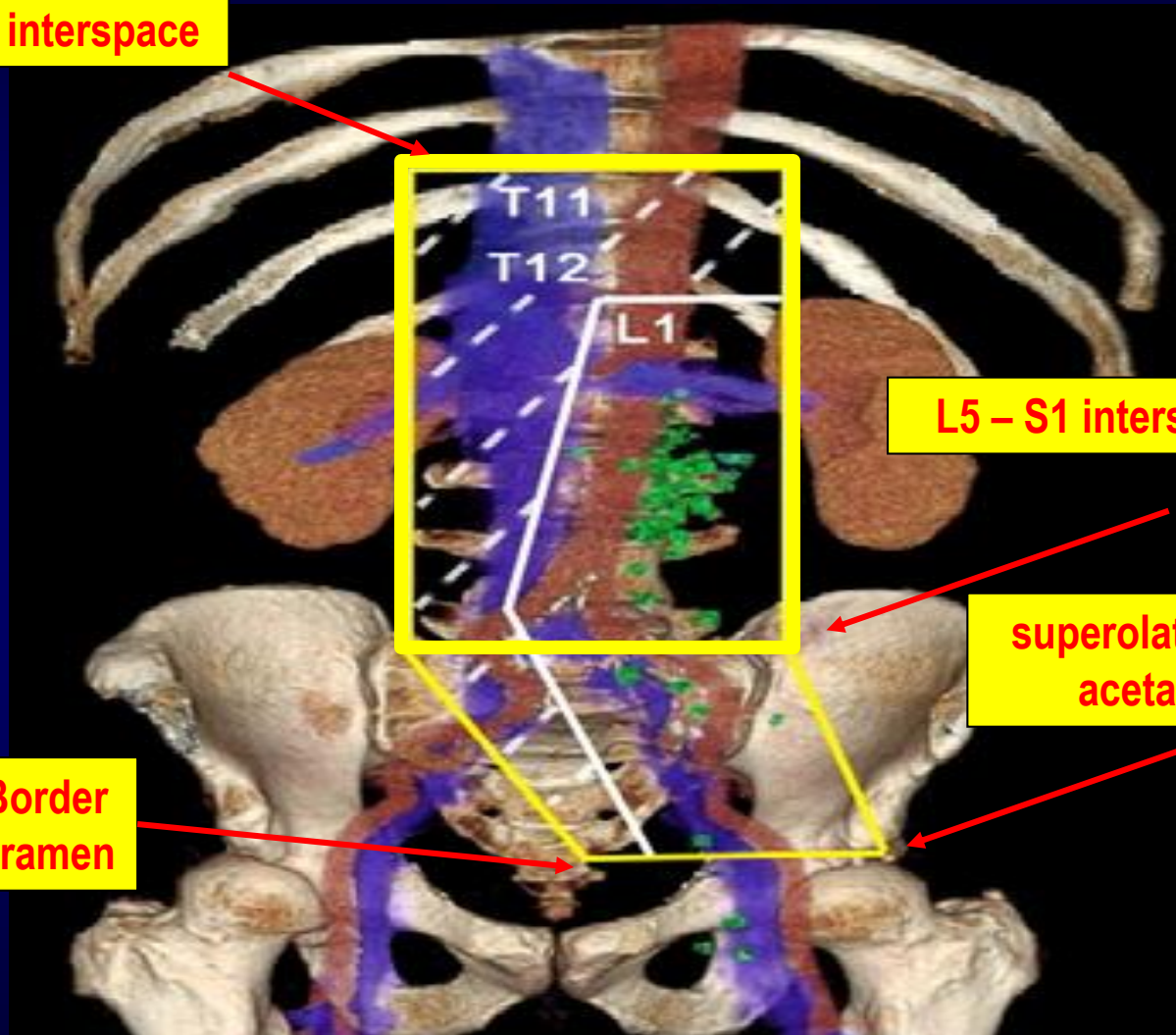
# Radiotherapy

- Classical Dog leg
  - History of inguinal herniorrhaphy or orchiopexy prior to inguinal orchiectomy
  - Alteration in lymphatic drainage
  - Include ipsilateral iliac and inguinal nodes
  - Include previous surgical scar
- Modified Dog Leg field – described by caseen



# PA & Modified Dog Leg

T10 – T11 interspace



L5 – S1 interspace

superolateral tip of  
acetabulum

Along Medial Border  
of obturator Foramen

# RT doses

Stage	Phase 1 Modified Dog Leg Or Dog Leg	Phase II boost to gross node (2 cm margin)	Dose per fraction
IIA	20 Gy	10 Gy	1.8 – 2 Gy/#
IIB	20 Gy	16 Gy	1.8 – 2 Gy/#

# RT fields

Figure 1:  
Stage I RT Field

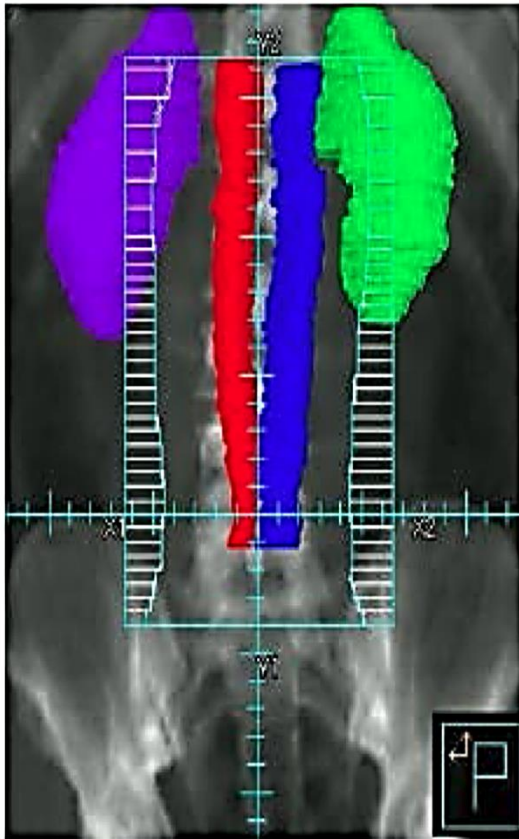
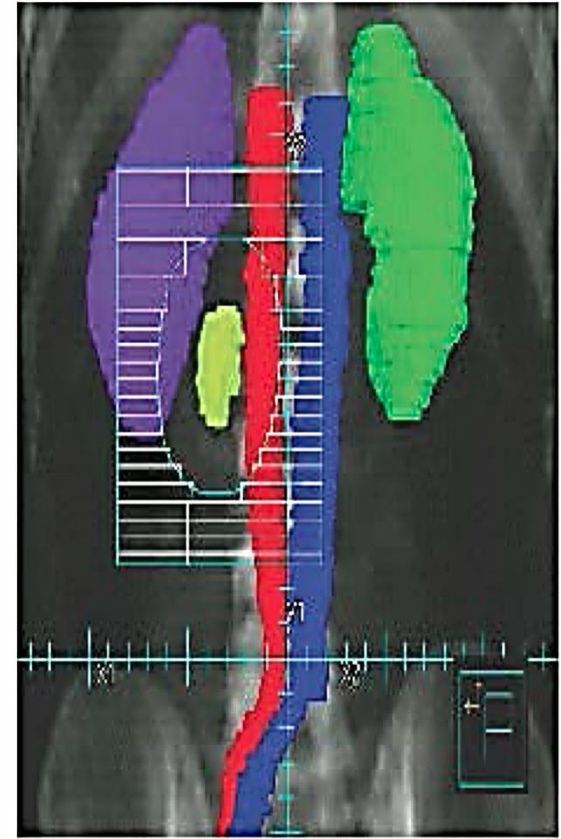


Figure 2:  
Stage II RT Large Field



Figure 3:  
Stage II Cone-down Field



# Stage IIA & IIB

- IIA
  - RT (total dose 30Gy) with modified Dog Leg field
  - Chemo - BEP x 3 Cycle or EP x 4 Cycles
- IIB
  - Chemo is favored BEP x 3 Cycle or EP x 4 Cycles
  - RT for less than 3 cm node RT (total dose 36Gy) with modified Dog Leg field
- **Avoid RT – Horseshoe kidney, Inflammatory Bowel Disease (IBD), history of RT**
- **Classical dog leg if history of inguinal herniorrhaphy or orchiopexy prior to inguinal orchiectomy**
- **Consider Bleomycin free regimen in patients**
  - **with reduced or Borderline GFR**
  - **Age >50 yrs**
  - **Compromised Lung function**

## II C & III

- Good Risk
  - BEP x 3 Cycle or EP x 4 Cycles
- Intermediate Risk
  - BEP x 4 Cycles
  - VIP x 4 Cycles
- **Consider Bleomycin free regimen in patients**
  - **with reduced or Borderline GFR**
  - **Age >50 yrs**
  - **Compromised Lung function**

### Preferred Regimens

BEP = Bleomycin/etoposide/cisplatin

EP = Etoposide/cisplatin

### Other Recommended Regimens

VIP = Etoposide/ifosfamide/cisplatin

# BEP VS VIP

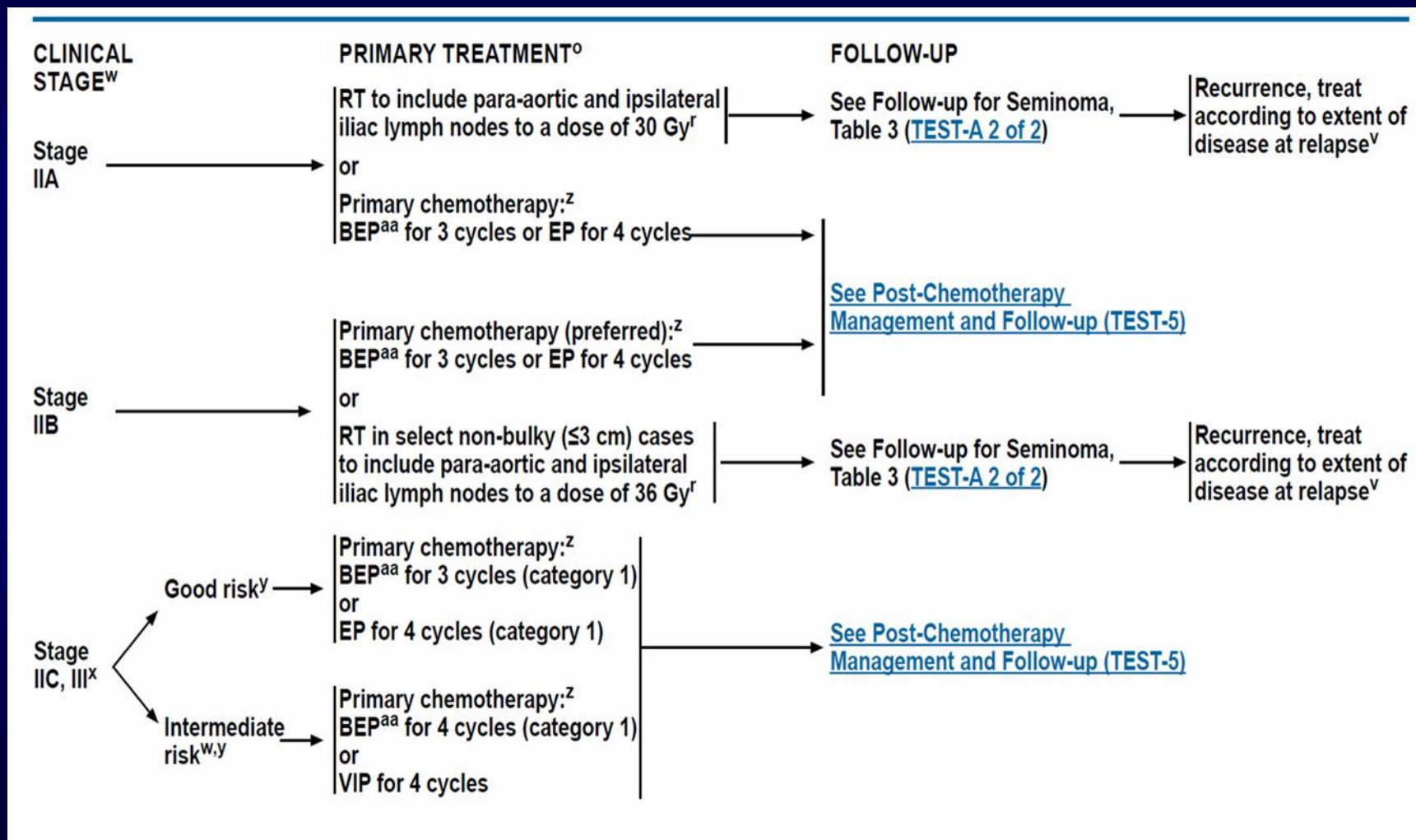
Author	Randomisation	OS rates (%)	PFS(%)	Complete remission (%)	Toxicity
Hinton S et al. 1987-1992 Follow up median 7.3yrs Update from ECOG/SWOG/CALGB group Intergroup	<b>BEP - 152</b>	<b>67</b>	<b>58</b>		<b>73</b> haematological
	<b>VIP - 152</b>	<b>69</b>	<b>64</b>		<b>89</b>
R de Wit et al. EORTC group Good Prognosis NSGCT Follow up median 7.7 yrs	<b>BEP – 131</b>	<b>95</b>	<b>83</b>	<b>79</b>	<b>37</b> neutropenia
	<b>VIP– 126</b>	<b>98</b>	<b>85</b>	<b>74</b>	<b>89</b>
Nichols CR et al 1987-1992 ECOG/SWOG/CALGB group	<b>BEP</b>	<b>71</b>	<b>60</b>	<b>31</b>	
	<b>VIP</b>	<b>74</b>	<b>64</b>	<b>37</b>	

# Stage I

CLINICAL STAGE	PRIMARY TREATMENT <sup>o</sup>	FOLLOW-UP
Stage IA, IB	Surveillance for pT1-pT3 tumors (strongly preferred)	See Follow-up for Seminoma, Table 1 ( <a href="#">TEST-A 1 of 2</a> ) → Recurrence, treat according to extent of disease at relapse <sup>v</sup>
	or	
	Single-agent carboplatin <sup>p,q</sup> (AUC=7 x 1 cycle or AUC=7 x 2 cycles)	See Follow-up for Seminoma, Table 2 ( <a href="#">TEST-A 1 of 2</a> ) → Recurrence, treat according to extent of disease at relapse <sup>v</sup>
	or	
	RT <sup>r</sup> (20 Gy or 25.5 Gy) <sup>s</sup>	See Follow-up for Seminoma, Table 2 ( <a href="#">TEST-A 1 of 2</a> ) → Recurrence, treat according to extent of disease at relapse <sup>v</sup>
Stage IS		Repeat elevated serum tumor marker measurement <sup>b</sup> and assess with chest/abdominal/pelvic CT (with contrast) to scan for evaluable disease <sup>t,u</sup> → Recurrence, treat according to extent of disease at relapse <sup>v</sup>



# Stage II-III



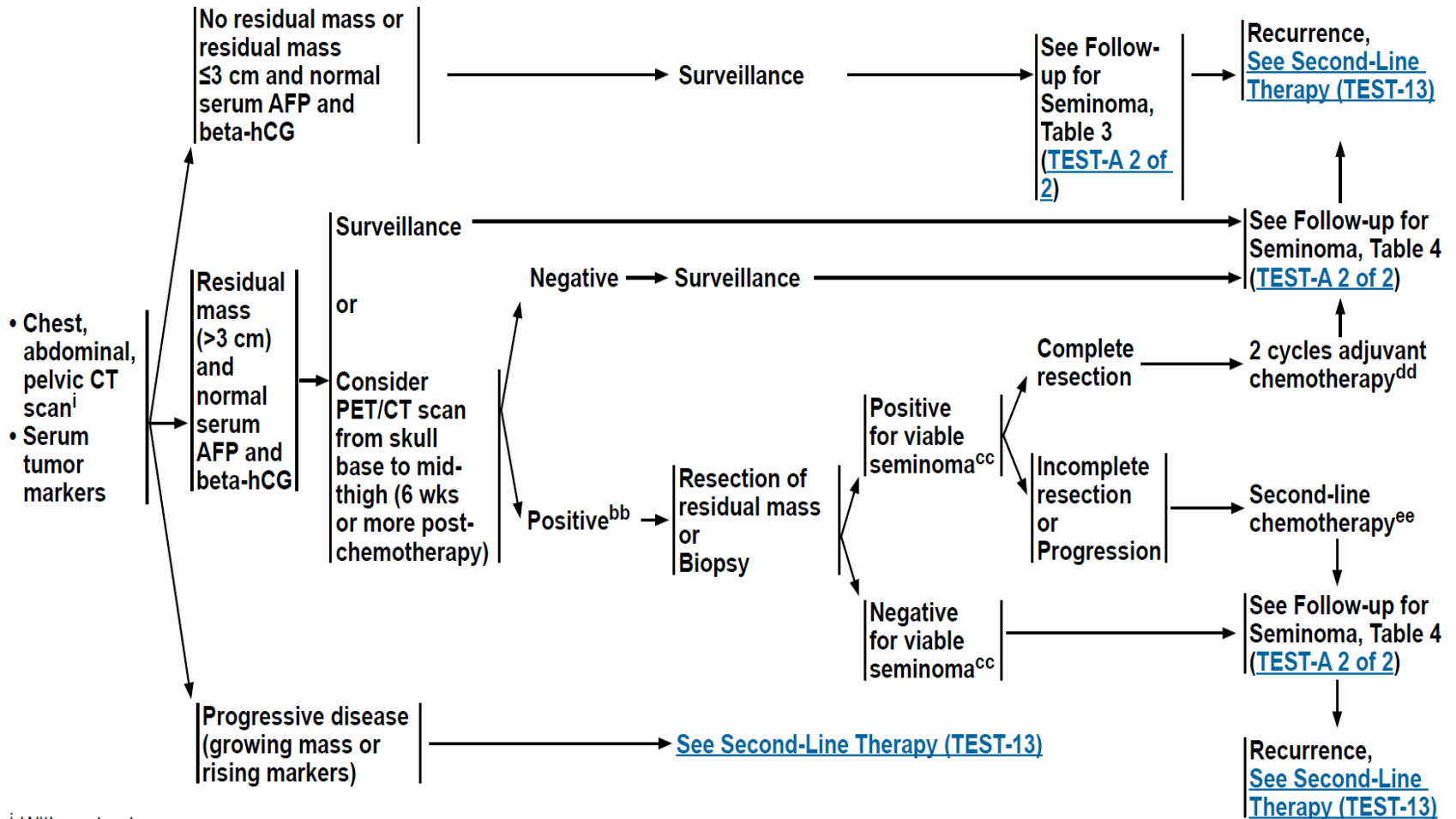


# After treatment of Chemotherapy

STAGE IIA, IIB, IIC, III AFTER PRIMARY TREATMENT WITH CHEMOTHERAPY

POST-CHEMOTHERAPY MANAGEMENT

FOLLOW-UP



<sup>i</sup> With contrast

# Follow up stage I

**Table 1 Clinical Stage I Seminoma: Surveillance After Orchiectomy**

	Year (at month intervals)				
	1	2	3	4	5 <sup>d</sup>
H&P <sup>a,b</sup>	Every 3–6 mo	Every 6 mo	Every 6–12 mo	Annually	Annually
Abdominal ± Pelvic CT <sup>c,e</sup>	At 3, 6, and 12 mo	Every 6 mo	Every 6–12 mo	Every 12–24 mo	
Chest x-ray	As clinically indicated, consider chest CT with contrast in symptomatic patients.				

If Recurrence, treat according to extent of disease at relapse

**Table 2 Clinical Stage I Seminoma: Surveillance After Adjuvant Treatment (Chemotherapy or Radiation)**

	Year (at month intervals)				
	1	2	3	4	5 <sup>d</sup>
H&P <sup>a,b</sup>	Every 6–12 mo	Every 6–12 mo	Annually	Annually	Annually
Abdominal ± Pelvic CT <sup>c,e</sup>	Annually	Annually	Annually	—	
Chest x-ray	As clinically indicated, consider chest CT with contrast in symptomatic patients				

If Recurrence, treat according to extent of disease at relapse

**Table 3 Clinical Stage IIA and Non-Bulky IIB Seminoma: Surveillance After Radiotherapy or Post-Chemotherapy<sup>f</sup>**

	Year (at month intervals)				
	1	2	3	4	5 <sup>d</sup>
H&P <sup>a,b</sup>	Every 3 mo	Every 6 mo	Every 6 mo	Every 6 mo	Every 6 mo
Abdominal ± Pelvic CT <sup>e,g</sup>	At 3 mo, then at 6–12 mo	Annually	Annually	As clinically indicated	
Chest x-ray <sup>h</sup>	Every 6 mo	Every 6 mo	—		

If Recurrence, treat according to extent of disease at relapse

**Table 4 Bulky Clinical Stage IIB, IIC, and Stage III Seminoma: Surveillance Post-Chemotherapy**

	Year (at month intervals)				
	1	2	3	4	5 <sup>d</sup>
H&P and markers <sup>b</sup>	Every 2 mo	Every 3 mo	Every 6 mo	Every 6 mo	Annually
Abdominal/ Pelvic CT <sup>e,g,h,i,j,k</sup>	Every 4 mo	Every 6 mo	Annually	Annually	As clinically indicated
Chest x-ray <sup>h</sup>	Every 2 mo <sup>l</sup>	Every 3 mo <sup>l</sup>	Annually	Annually	Annually

If Recurrence, [see TEST-13](#).

# RT vs Chemo

THANK YOU