

Primary RPLND for stage II seminoma

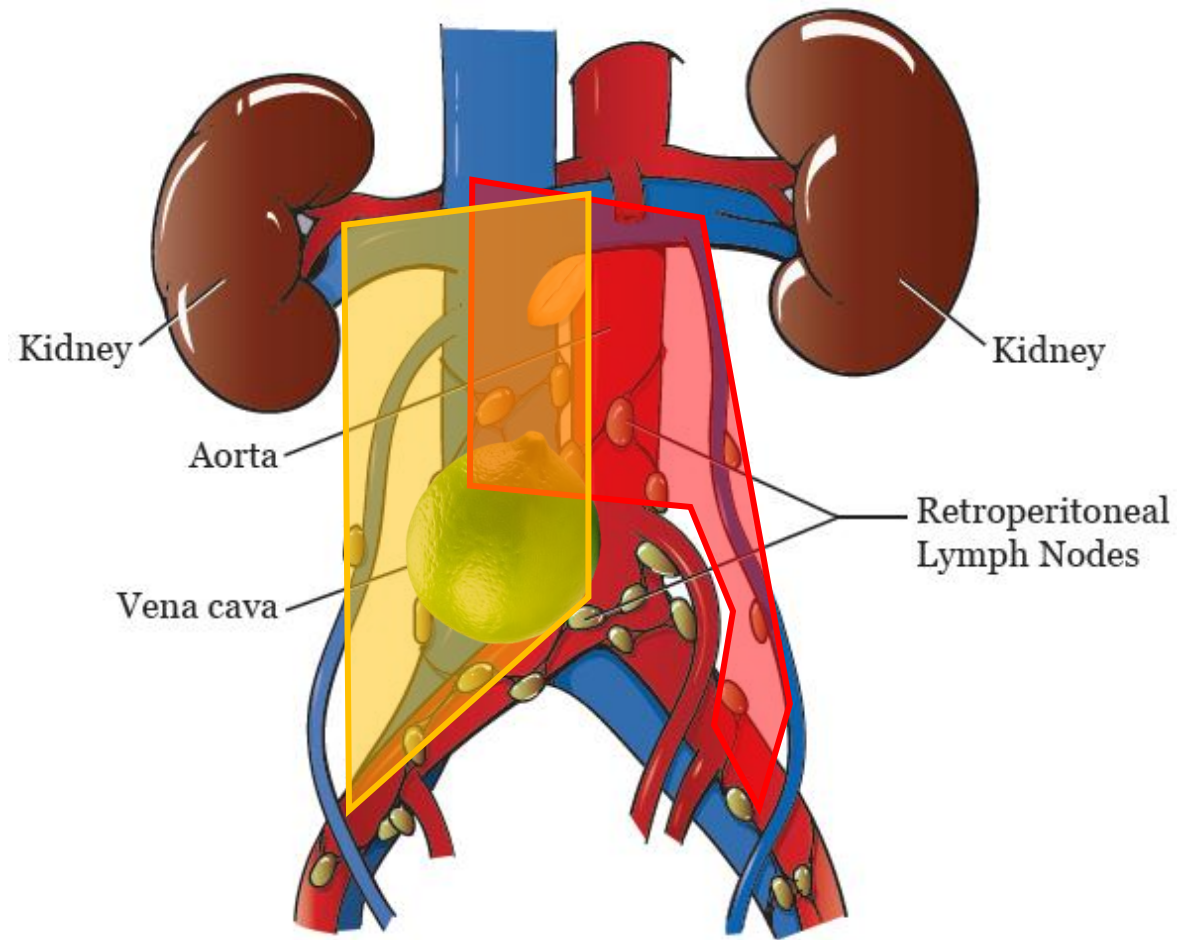
Thomas Van den Broeck
16-05-2025



ZIEKENHUIS^{aan}
deSTROOM

I have no conflicts of interest

Stage IIA/B seminoma testis

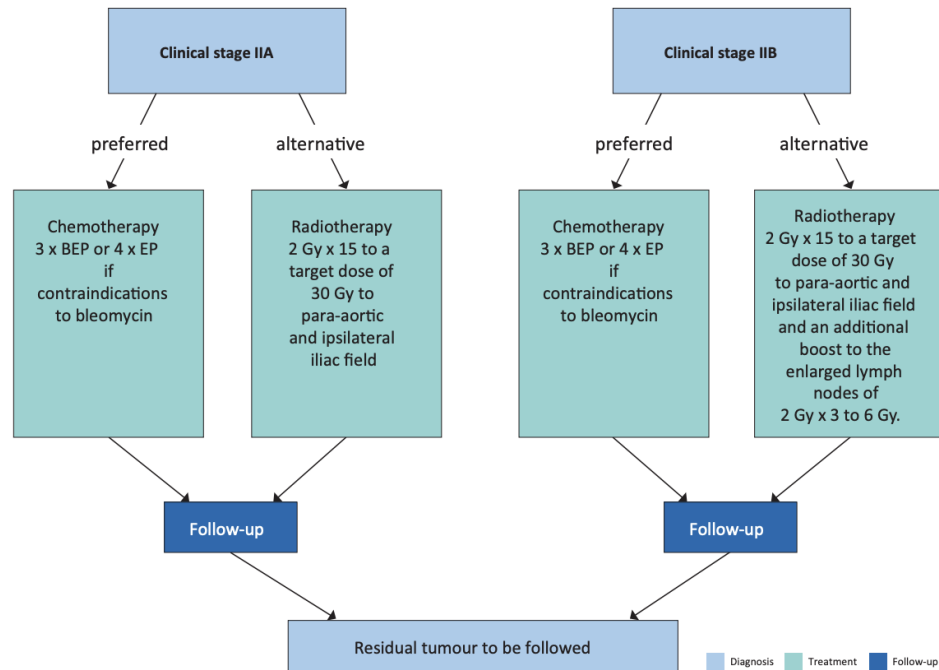


Stage IIA – N1 (<2 cm) S0/S1

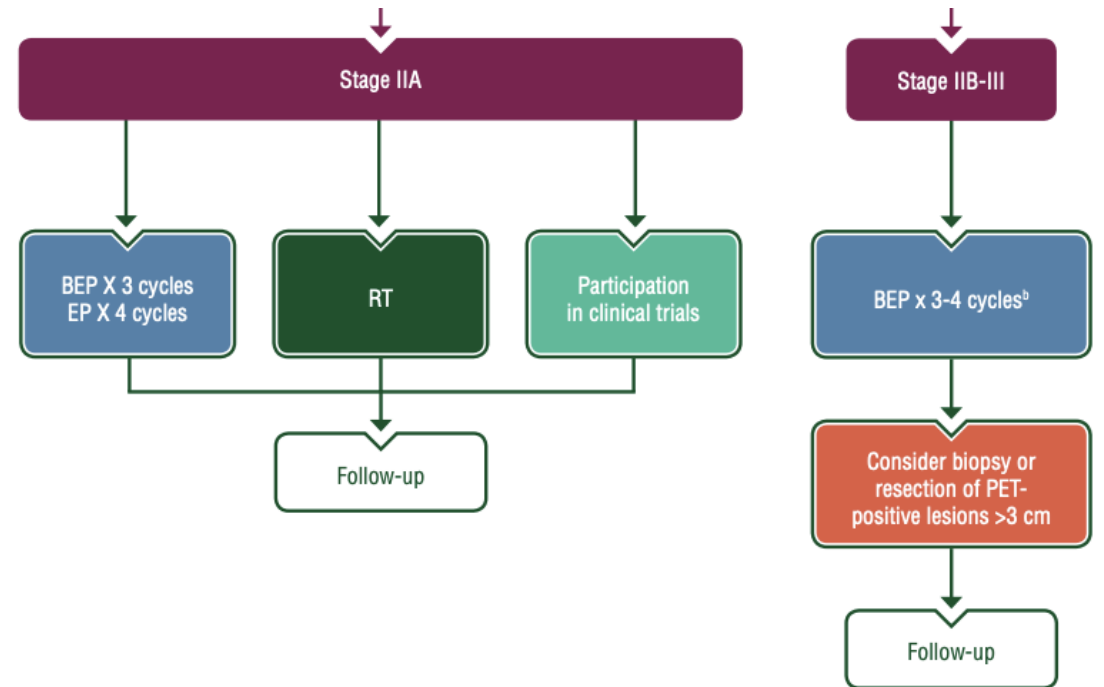
Stage IIB – N2 (2-5 cm) S0/S1

Standard of Care Treatment

EAU Guidelines

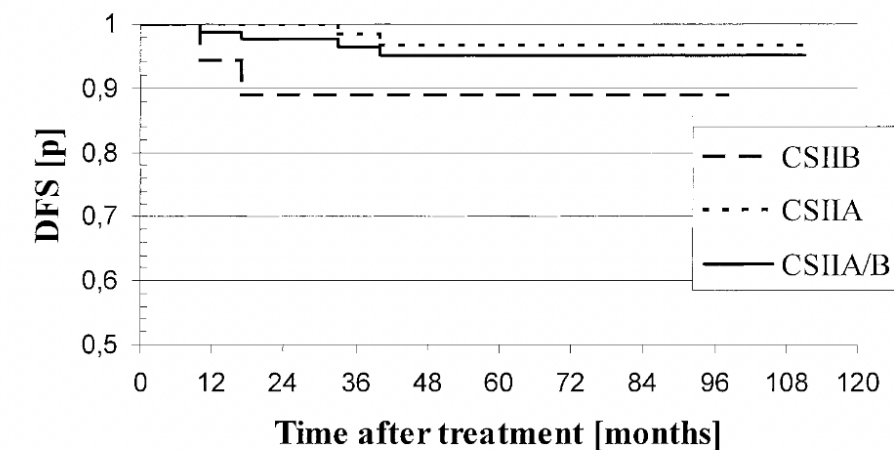


ESMO Guidelines



SoC - Efficacy

Radiotherapy



Pts. at risk

CSIIA	66	64	61	59	53	42	34	22	14	2	0
CSIIIB	21	17	17	16	12	11	10	5	2	0	0

Chemotherapy

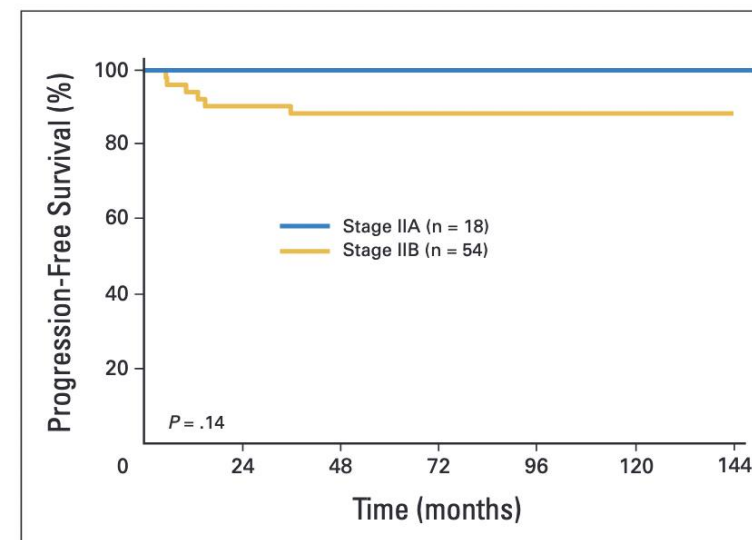


Fig 1. Progression-free survival curve for patients with stage IIA and IIB testicular seminoma treated with cisplatin-based chemotherapy.

Classen J et al. JCO 2003.

Chun PW et al. Eur Urol 2004.

Garcia-del-Muro X et al. 2008 JCO.

SoC - Efficacy

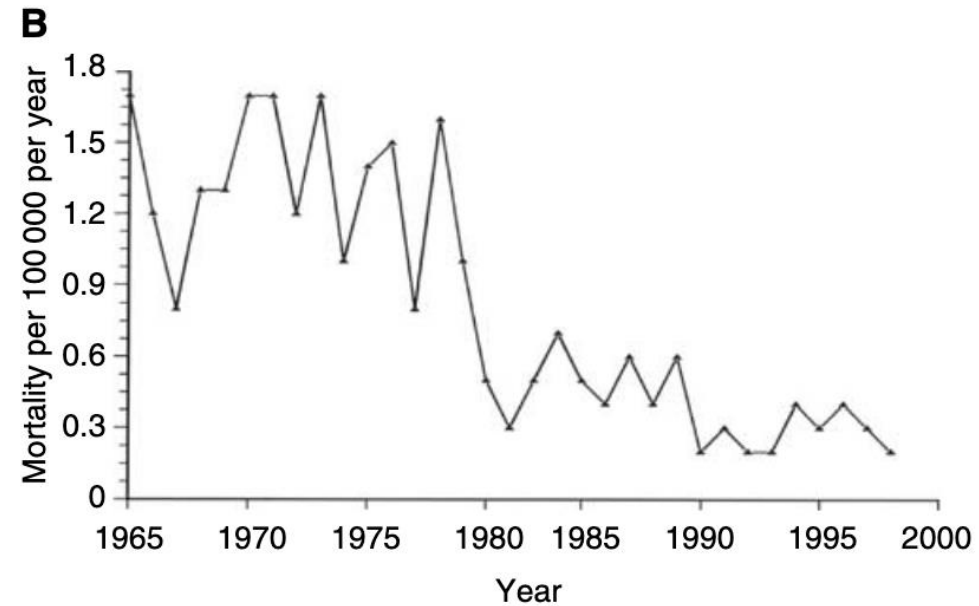


Figure I Age-adjusted (Based on World Standard population) incidence (**A**) and mortality (**B**) rates for patients with malignant germ cell tumours diagnosed from 1965 to 1999 (The Cancer Registry of Norway, personal communication, 2002).

SoC – Overtreatment?

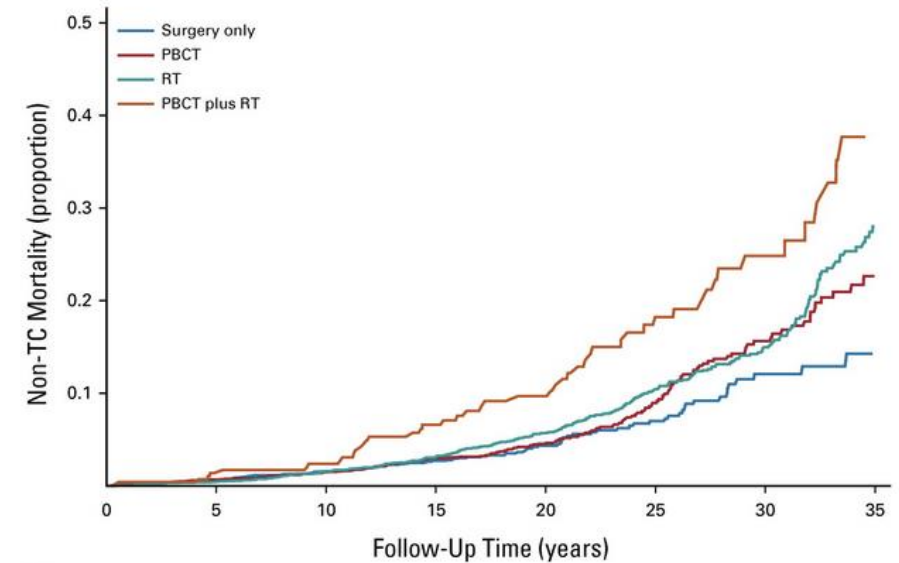
TABLE 5. HRs for Total Non-TC Mortality and Non-TC SC Mortality According to Treatment Groups, Treatment Intensity, and Histology After > 10 Years of Follow-Up

Variable	All Non-TC Mortality		Non-TC SC Mortality		Follow-Up, Years, Median (IQR)
	Age-Adjusted HR (95% CI)	Multivariable HR (95% CI)	Age-Adjusted HR (95% CI)	Multivariable HR (95% CI)	
Treatment groups					
Surgery	1 (ref)	1 (ref)	1 (ref)	1 (ref)	16.8 (12.1-24.0)
PBCT	1.42 (1.05 to 1.91)	1.42 (1.05 to 1.91)	1.69 (1.05 to 2.73)	1.69 (1.05 to 2.73)	16.8 (11.6-23.9)
RT	1.61 (1.23 to 2.12)	1.94 (1.39 to 2.73)	1.87 (1.20 to 2.90)	1.83 (1.07 to 3.14)	23.3 (17.7-28.8)
PBCT plus RT	2.79 (1.89 to 4.13)	3.27 (2.14 to 5.00)	3.95 (2.22 to 7.02)	3.89 (2.06 to 7.33)	17.0 (3.7-26.3)

Table 3. Multivariate Cox Regression Analyses of Potential Risk Factors for SMNs and CVD

Risk Factor	SMN* (n = 263)		CVD*† (n = 251)		SMN and/or CVD*† (n = 435)		SMN and CVD*‡ (n = 43)	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
All treatments§								
Surgery only	1.0		1.0		1.0		1.0	
Subdiaphragmatic RT only	2.6	1.7 to 4.0	1.2	0.9 to 1.7	1.8	1.3 to 2.4	2.4	0.8 to 6.9
Subdiaphragmatic and mediastinal RT only	3.6	2.1 to 6.0	3.0	2.0 to 4.6	3.7	2.6 to 5.2	7.1	2.1 to 24.4
PVB/BEP, no RT¶	2.1	1.4 to 3.1	1.7	1.1 to 2.5	1.9	1.4 to 2.5	2.7	0.9 to 8.4
Smoking#								
Yes (v no or unknown)	1.8	1.3 to 2.4	1.8	1.3 to 2.4	1.7	1.4 to 2.1	3.4	1.8 to 6.4
RT dose**								
Surgery only	1.0		1.0		1.0			
Subdiaphragmatic RT only, 26-35 Gy	2.3	1.5 to 3.6	1.2	0.8 to 1.9	1.7	1.2 to 2.3		
Subdiaphragmatic RT only, 40-50 Gy	3.2	2.1 to 5.1	1.2	0.8 to 1.9	2.0	1.4 to 2.8		
P _{TREND} ††	< .001							

A



No. at risk:								
Surgery only	5,611	1,413	1,264	842	499	322	172	65
PBCT	91	2,391	2,169	1,416	953	559	304	113
RT	5	1,541	1,478	1,334	1,023	639	318	91
PBCT plus RT	0	130	138	123	98	69	37	14

Hellesnes R et al. JCO
van den Belt-Dusebout et al. JCO 2007.

SoC - Toxicity

Radiotherapy

Poorly reported

Mostly intestinal toxicity

Secondary malignancies:
- 15-year risk: 6-8%
- 30-year risk: 16%
Most occur in irradiated field

*Bauman G et al. Int J Radiat Oncol Biol Phys 1998.
Garcia-Serra et al. Am J Clin Oncol 2005.
Hallemeyer et al. Urol Oncol 2013.*

Chemotherapy

43% grade 3/4

Irreversible neuro- and ototoxicity: 16%
Restrictive lung-disease: 17%

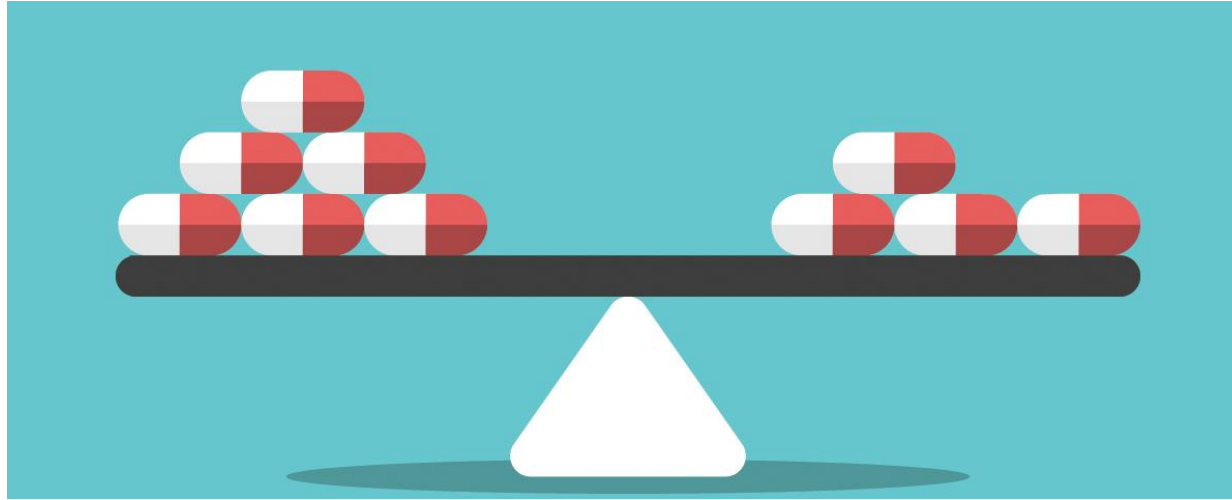
Long-term excess mortality (comparable to smoking)

*Classen J et al. JCO 2003.
Garcia-del-Muro X et al. 2008 JCO.
Maroto P et al. Crit Rev Oncol. 2018.
Mykletun A et al. JCO 2005.*

*Haugnes HS et al. JCO 2009.
Hellessness et al. Br J Cancer 2004
van den Belt-Dusebout et al. JCO 2007.*



Search for treatment de-escalation



De-escalate
chemotherapy

De-escalate
radiotherapy

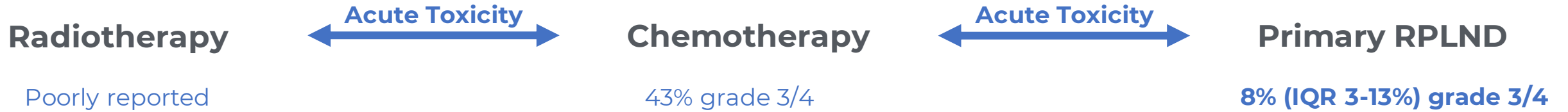
Primary RPLND

Primary RPLND – Increasing evidence

Author	n=	Adjuvant Rx	Recurr ence rate	Recurrence site	Clavien Dindo ≥ III	Rx for relapse	FU (months)
Daneshmand S 2023 (SEMS)	55	1x Carboplatinum pN2	22% (n=12)	Infield: 5 Outfield: 7	2% (n=1)	CT (83%), Surgery (17%)	33
Heidenreich A 2023 (COTRIMS)	30	NO	10% (n=3)	Outfield: 3	13% (n=4)	CT (100%)	22
Hiester A 2022 (PRIMETEST)	33	NO	30.3% (n=10)	Infield: 3 Outfield: 7	12% (n=4)	CT (100%)	32
Tachbana I 2023	67	2x EP for IIB	16.9% (n=11)	Infield: 1 Outfield: 10	9% (n=6)	CT (91%), CT + surgery (9%)	22
Thor A 2024	62	Mk+ - 3xBEP >2 LNs or >3 cm: 1x BEP	10% (n=6)	Infield: 4 Outfield: 2	5% (n=3)	NR	23

Daneshmand S et al. ASCO 2022.
Heidenreich A et al. ASCO 2022.
Hiester A et al. Eur Urol 2022.
Tachibana I et al. JCO. 2023.
Thor A et al. EUOS. 2024.

Reduction in toxicity



Late Toxicity and **very late toxicity** driven by need of **adjuvant/salvage chemotherapy**:

Overall burden of chemotherapy was reduced in 23/33 patients (PRIMETEST)

In 11% (IQR 9-16%) of patients: pN0 final histopathology. Without surgery would have received chemotherapy

Adjuvant treatment less toxic (1x Carboplatinum for pN2 (**SEMS**), 2x EP for IIB (**Tachbana**), >2 LNs or >3 cm: 1x BEP (**Thor**))

Adjuvant treatment **reserved for pN2 (stage IIB)** disease

Salvage treatment **NOT** more toxic

Recurrence Rates

Radiotherapy & Chemotherapy

+/- 5%



Primary RPLND

22% (IQR: 13-32%)

No clear difference between IIA and IIB disease (**CAVE:** IIB often adjuvant treatment)

All patients who underwent salvage treatment: **remission at end of study**

CAVE: Average follow-up 26 months (IQR 22-33)

Uncertainties

Surgical approach

Open/robot?

Template?

How does surgery compare to de-escalation of

Chemotherapy?
(GETUG SEMITEP)

Radiotherapy?
(SAKK 01/10)

Who should get adjuvant treatment?

No one?
(COTRIMS, PRIMETEST)

IIB?
(SEMS, Tachbana, Thor)

Role of biomarkers?

Conclusions

Chemotherapy and radiotherapy remain SoC treatments

Long-term toxicities in current regimens are **no longer acceptable**

Surgery significantly **reduces toxicity** at the expense of a **higher recurrence rate**

Short to intermediate follow-up suggests **oncological safety**