

Stage IIA-IIB Seminoma Treatment Options: Radiation Therapy

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**12th Belgian Multidisciplinary
Meeting on Urological Cancers**

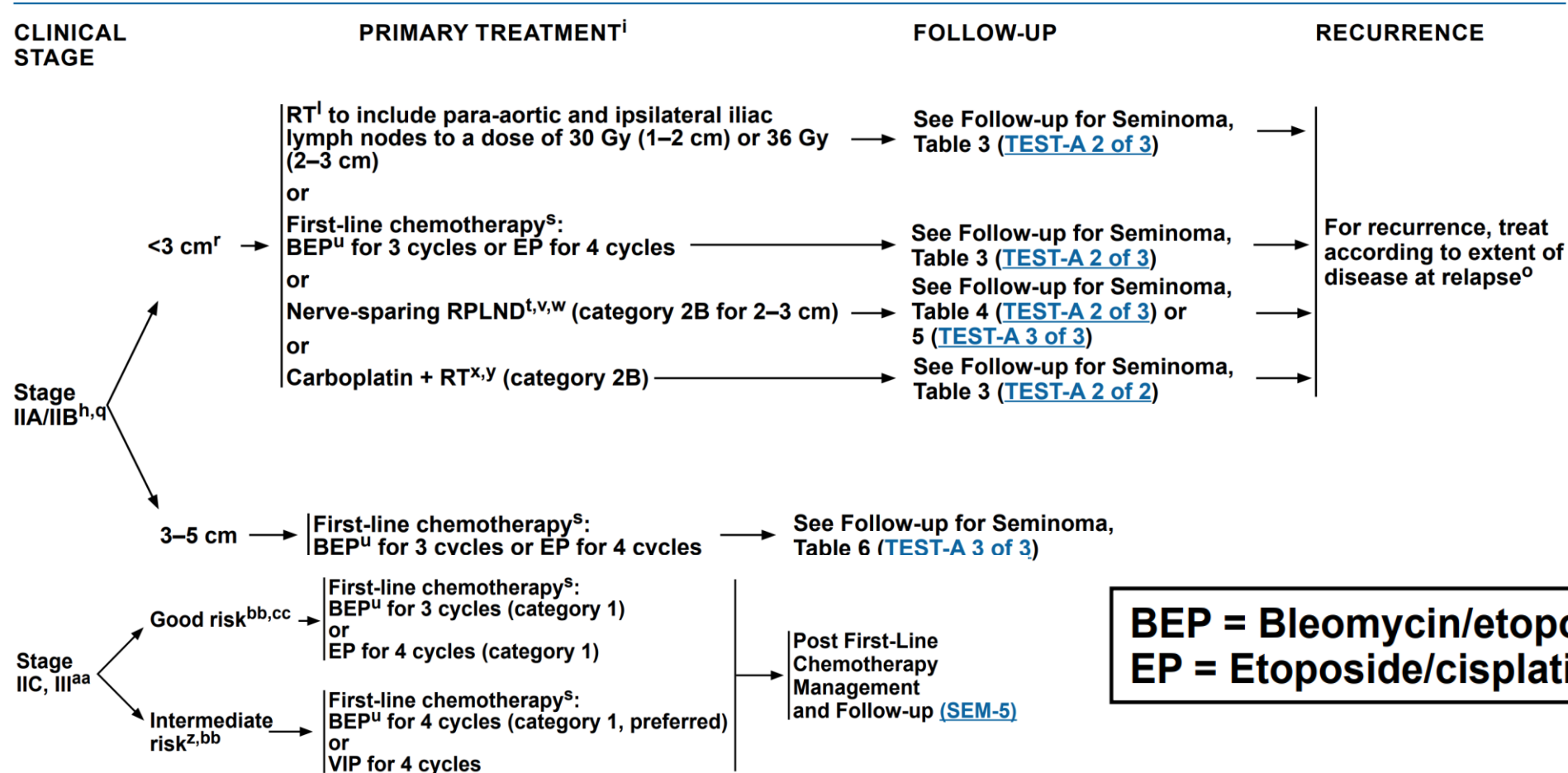
Conflicts of interest

- I have the following potential conflict(s) of interest to report

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports:	Merck, Myriad Genetics
Receipt of honoraria or consultation fees:	Lantheus, Telix, Boston Scientific, Molli Surgical, Vision RT, Elekta, Bayer
Participation in a company sponsored speaker's bureau:	NA
Stock shareholder:	NA
Spouse/partner:	NA
Other support (please specify):	Editor of MD Anderson Handbook of Radiation Oncology, published by Wolter Kluwer (1 st and 2 nd Editions)



NCCN Guidelines: Stage II Seminoma



BEP = Bleomycin/etoposide/cisplatin
EP = Etoposide/cisplatin

Radiation for IIA/B: Classen et al.

Stage IIA or IIB
n=94

Radiation therapy
30 Gy for stage IIA
36 Gy for stage IIB

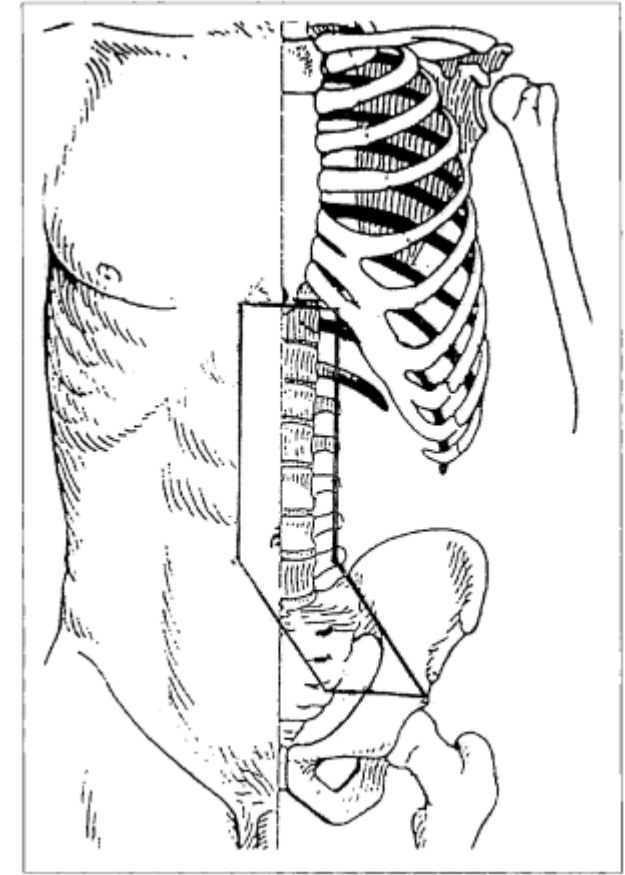
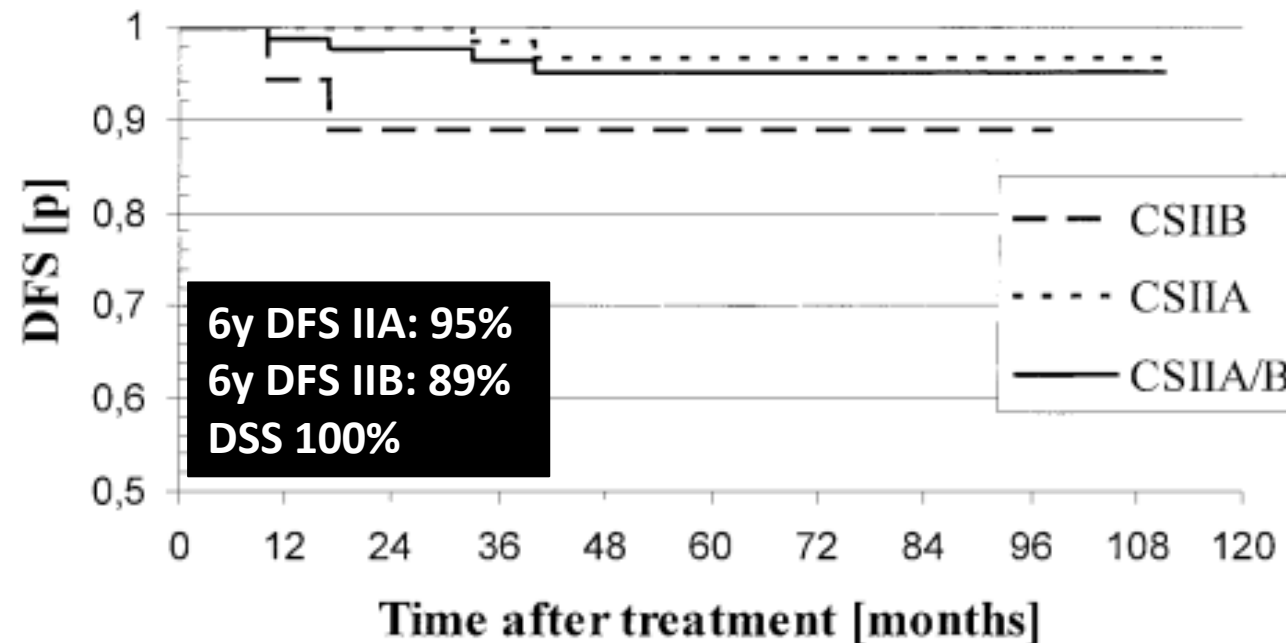


Fig 1. Treatment portals used for treatment of stage IIA and IIB seminoma.

Classen et al. Results

Disease Free Survival
Median FU: 70 months



Toxicity

No grade 4-5

Early Toxicities

8-10%: Grade 3 Nausea

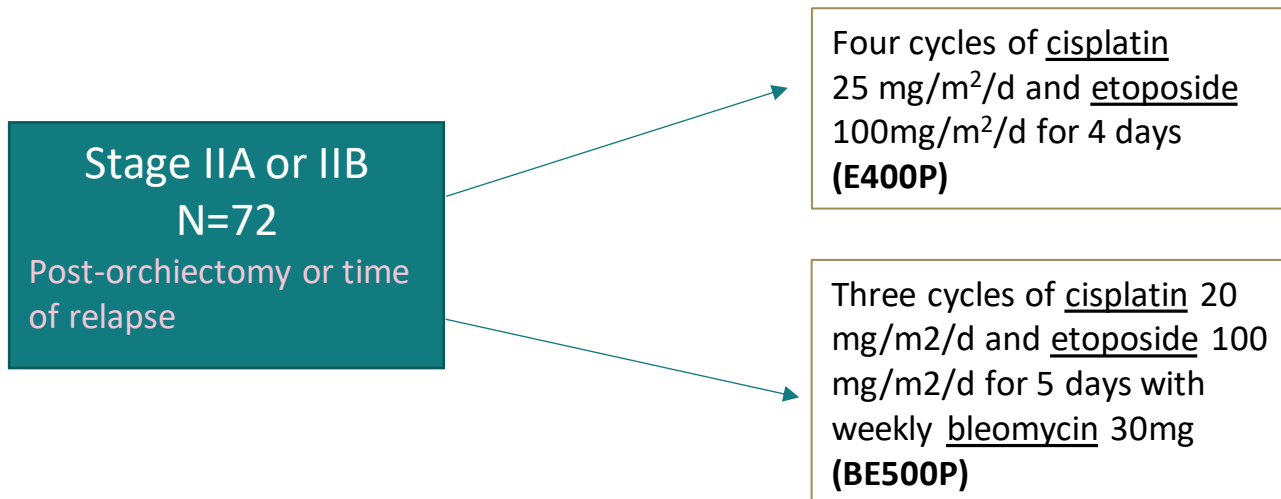
6-10%: Grade 3 Diarrhea

Late Toxicities

1 Skin hyperpigmentation

No secondary malignancies

Spanish Germ Cell Cancer Group: Chemotherapy



Characteristic	No. of Patients (N = 72)	%
Age, years		
Median	32	
Range	23-66	
Stage		
IIA	18	25
IIB	54	75
Disease at start of treatment		
Metastatic on diagnosis	59	82
Relapse of stage I on surveillance	13	18

Spanish Germ cell Cancer Group: Chemotherapy

Median FU: 71.5 months

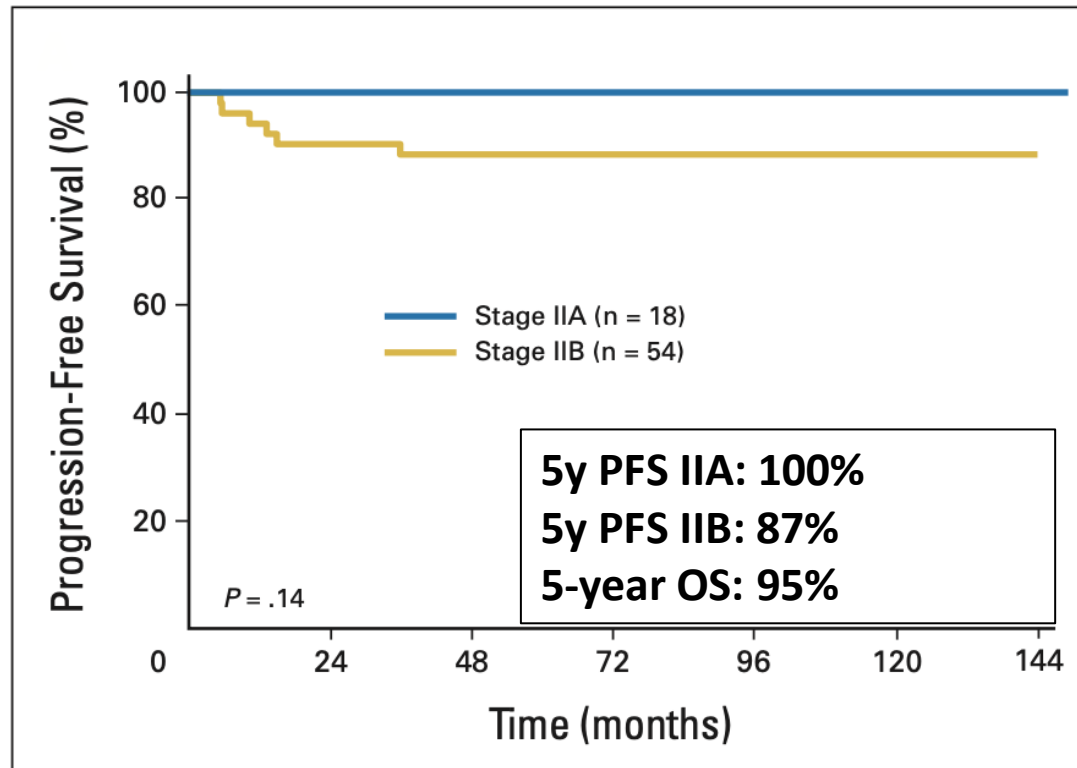


Table 2. Worst Toxicity by Patient

Toxicity	Grade 3 or 4		All Grades	
	No. of Patients	%	No. of Patients	%
Granulocytopenia	9	13	27	38
Thrombocytopenia	2	3	9	13
Anemia	1	2	4	6
Febrile neutropenia	8	11	8	11
Vomiting	6	8	33	46
Mucositis	1	2	6	8
Diarrhea	1	2	2	3
Pulmonary toxicity	1	2	1	2
Peripheral neuropathy	—	—	14	19
Rash	—	—	3	4
Ototoxicity	—	—	2	3
Alopecia	—	—	72	100

SEMS: RPLND in stage II seminoma

Stage IIA or IIB
N=55, Post-orchietomy
or time of relapse
LN <3cm; ≤2 cLNs

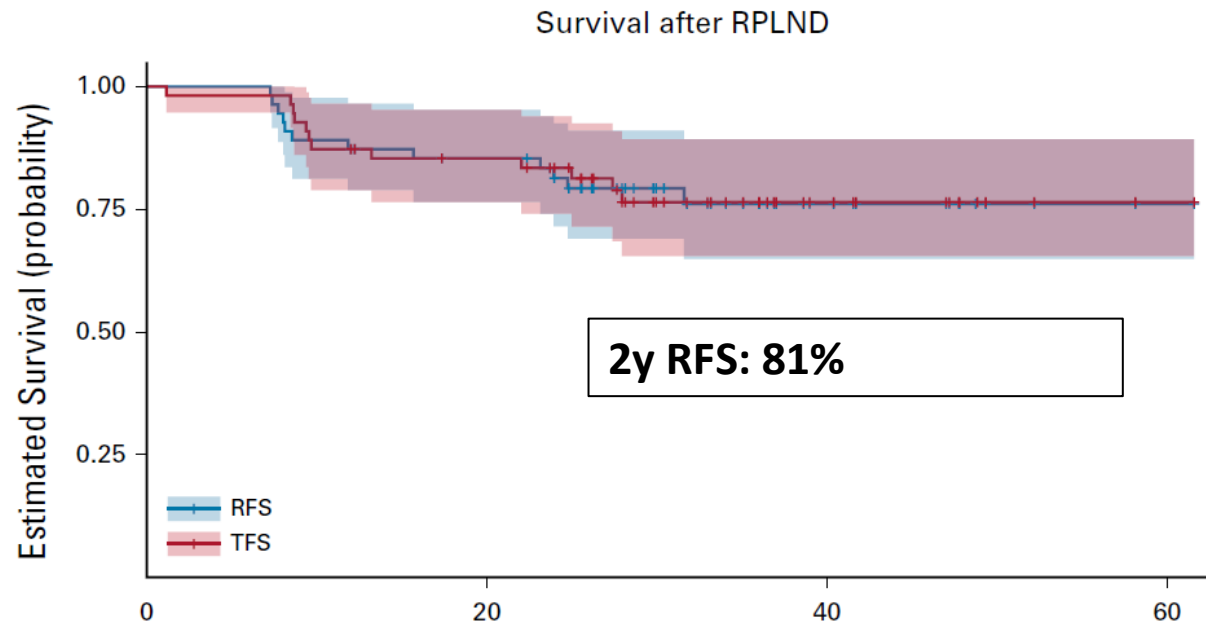


Open RPLND

Clinical stage, No. (%)	
Stage I with recurrence (1-2 cm)	27 (49)
Stage I with recurrence (>2 cm)	9 (16)
Stage IIA	17 (31)
Stage IIB	2 (4)
No. of clinically enlarged lymph nodes, No. (%)	
One	40 (73)
Two	15 (27)

SEMS: Results

Median follow-up: 33 mo



Toxicities:

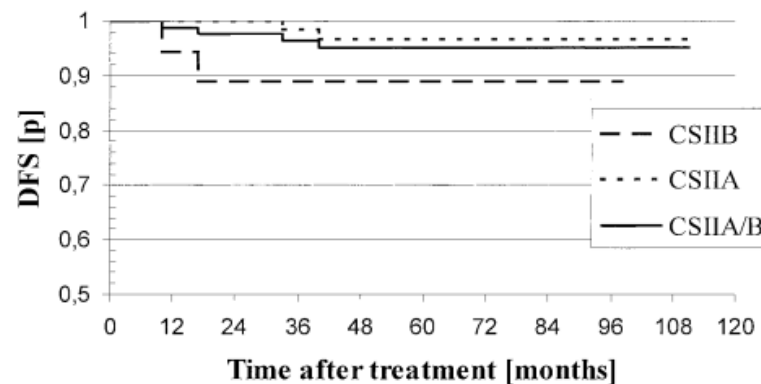
7% short-term

7% long-term (hernia, anejaculation)

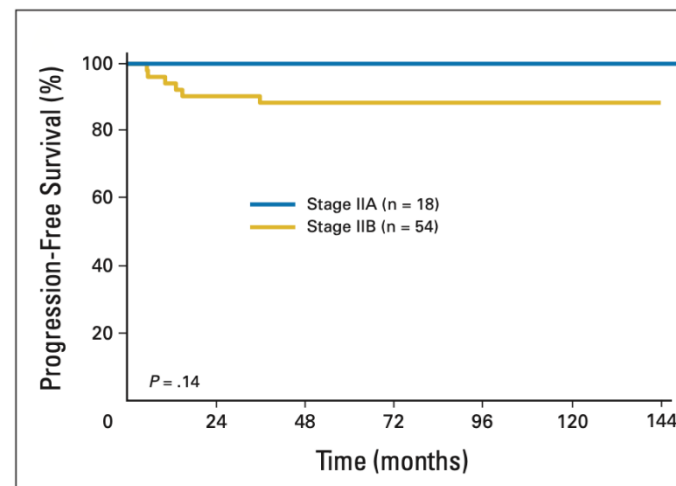
Efficacy Comparison

	Population	Median FU
Radiation <i>Classen</i>	75%: IIA 25%: IIB	70 Months
Chemotherapy <i>Spanish</i>	25%: IIA 75%: IIB	71.5 Months
RPLND <i>SEMS</i>	35%: IIA/B 65%: Stage I Recurrence	33 Months

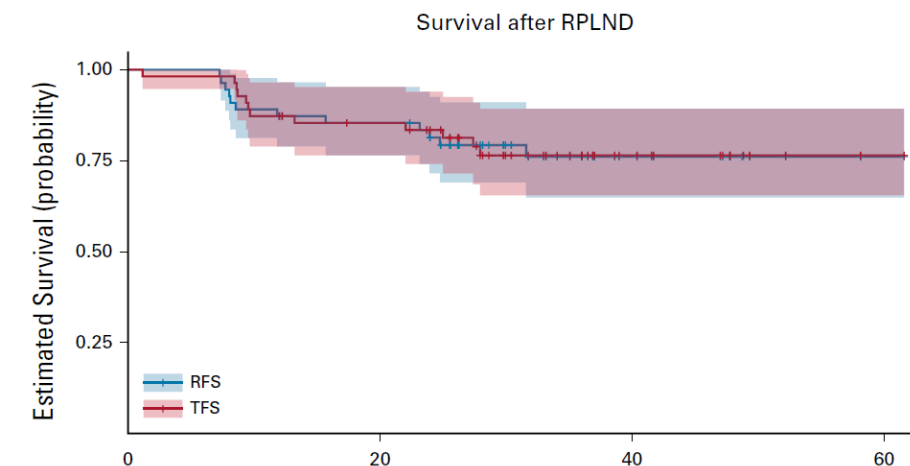
Radiation



Chemotherapy



RPLND





Radiation Therapy



JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Secondary malignancies after treatment of testicular germ cell tumors: a systematic review & meta-analysis

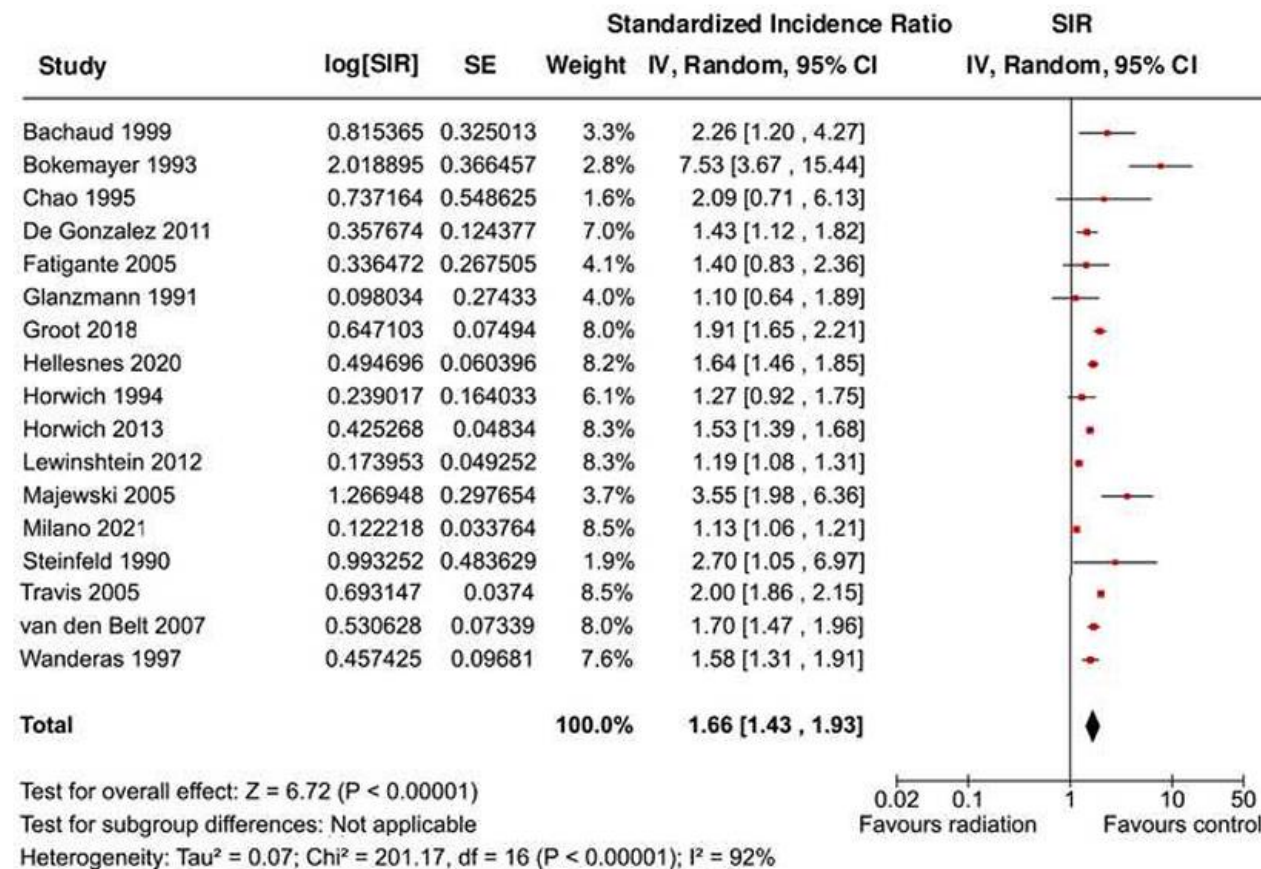
Ahmad Mousa, MD ✉ , Ali Amiri, MD, PhD , Sanchit Kaushal, BSc ,
Emma Wilson, MLIS, BHSc , Viranda Jayalath, MD, MSc , David-Dan Nguyen, MD, MPH ,
Isabelle Tan, BSc , Robert J Hamilton, MD, MPH

JNCI: Journal of the National Cancer Institute, djaf099,
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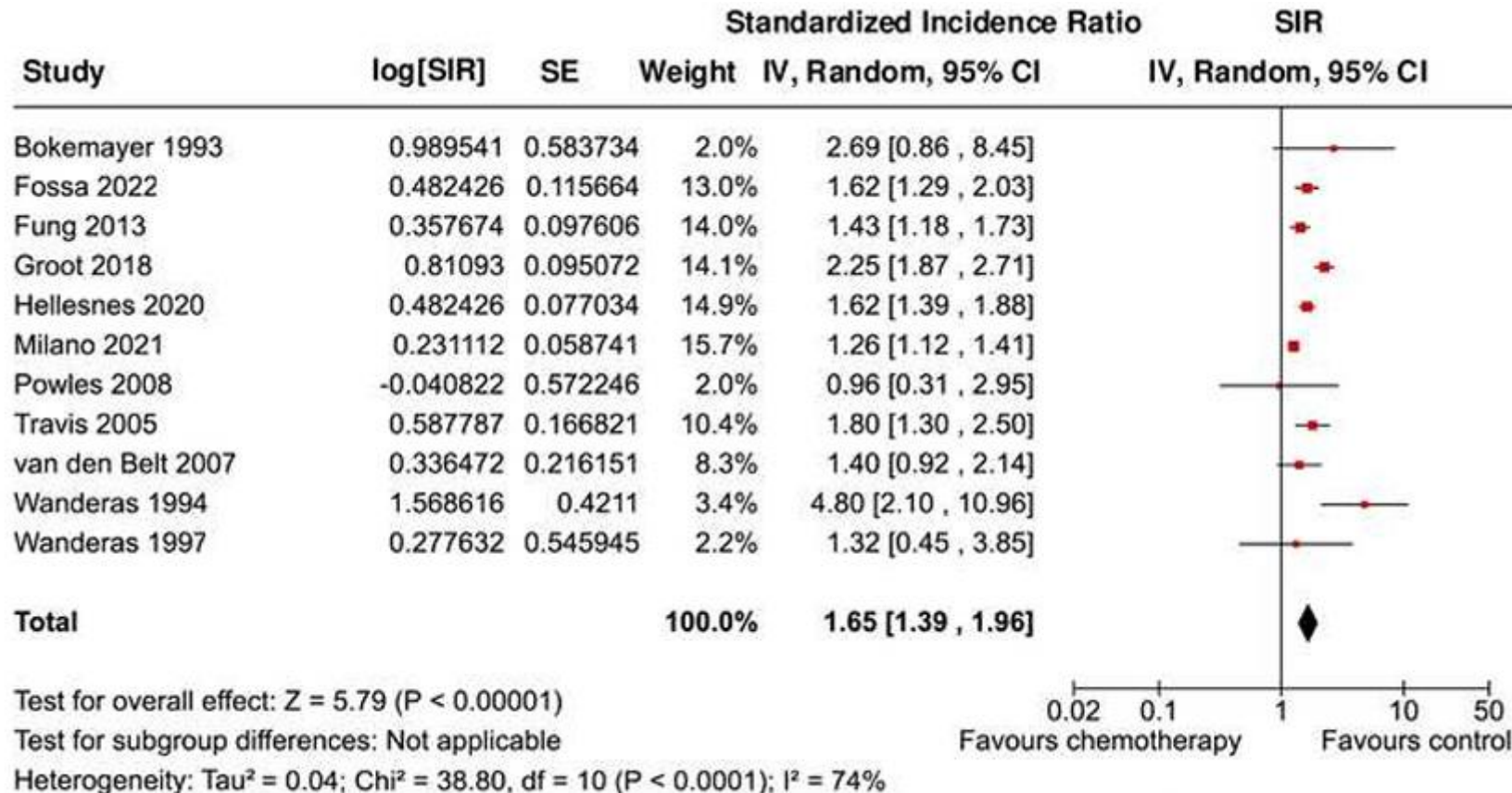
Meta-Analysis: Second malignancy after RT

- Radiation: 17 studies evaluating 44,135 patients



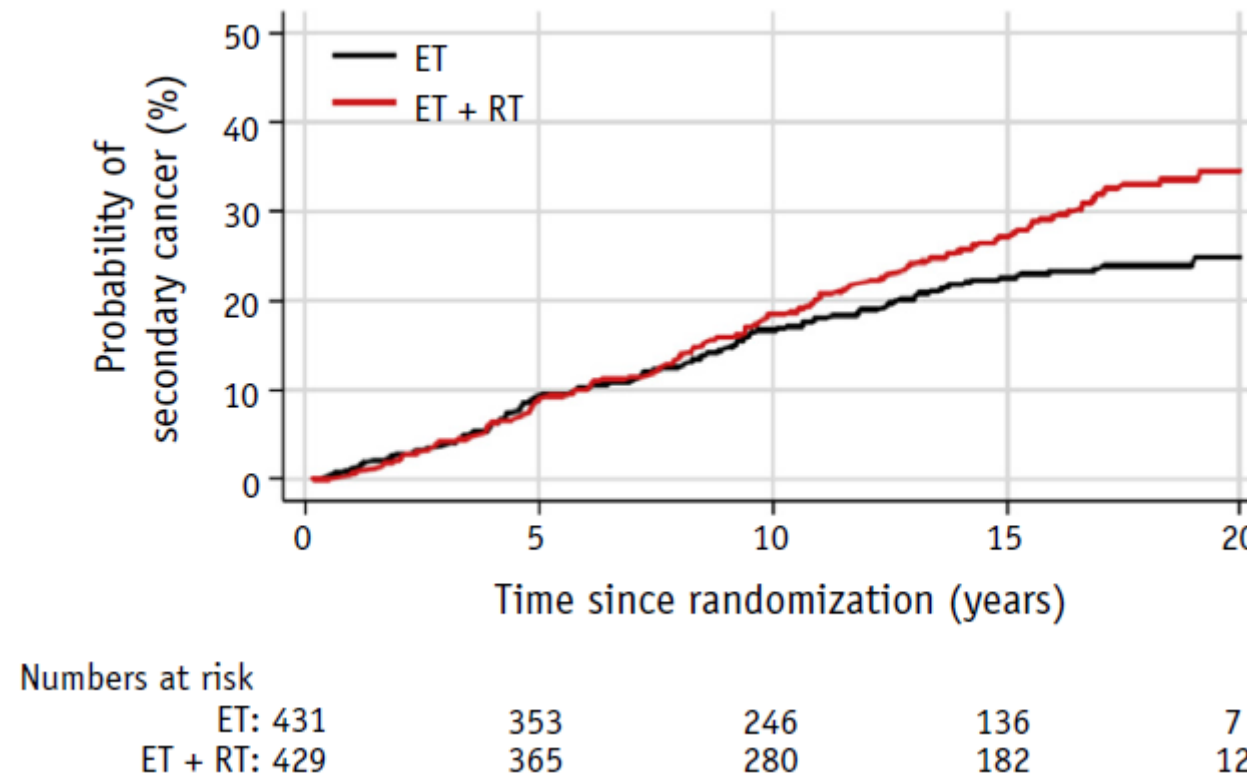
Meta-Analysis: Second malignancy after RT

- Chemotherapy: 11 studies with 23,851 patients



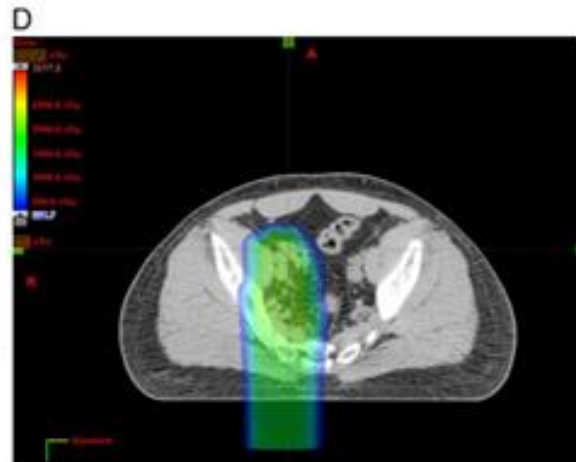
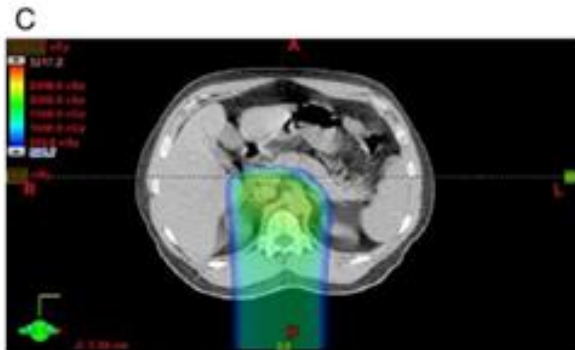
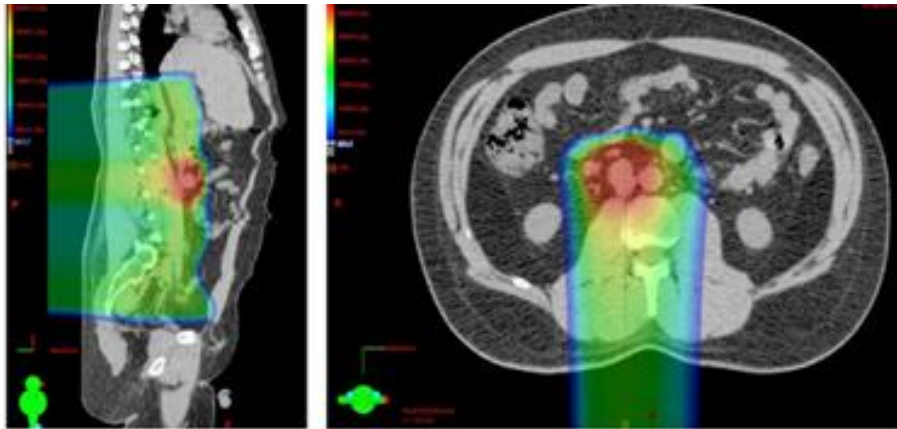
Secondary malignancies over time

- Randomized study of hormone therapy +/- radiation for prostate in SPCG 7 study, median FU of 12.6 years

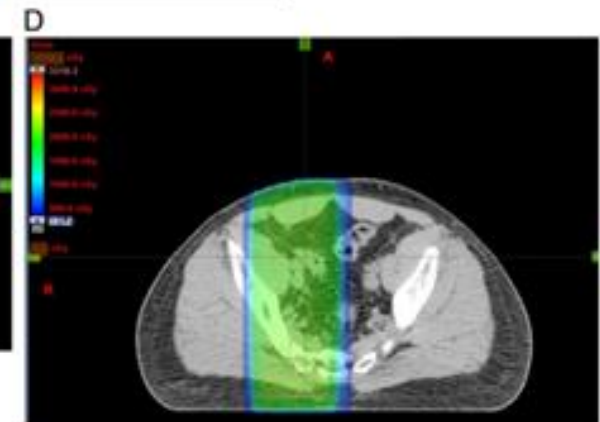
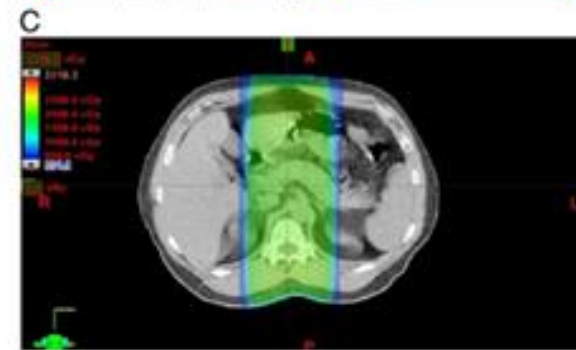
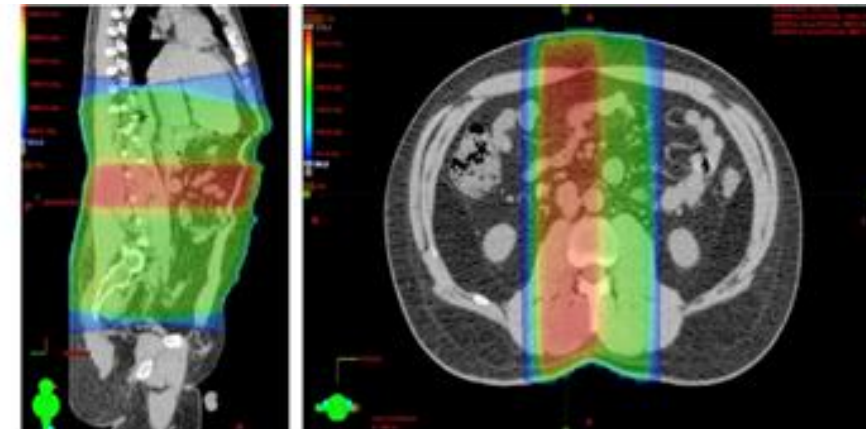


Proton therapy benefit?

Proton Therapy Plan



Photon Plan



Comparison: Proton vs Photon

Toxicities during radiation therapy treatment.

	PBT-Arm (n = 11), % (n)		XRT-Arm (n = 44), % (n)	P value ^a
Nausea and/or emesis	54.5 (6)		75.0 (33)	.182
Grade 1	45.5 (5)		75.0 (33)	
Grade 2	9.1 (1)		0	
Diarrhea	0		29.5 (13)	.039
Grade 1	0		25.0 (11)	
Grade 2	0		4.5 (2)	
Dermatitis (grade 1)	27.3 (3)		2.3 (1)	.004
Dysuria (grade 1)	0		0	1.000
Fatigue (grade 1)	45.5 (5)		22.7 (10)	.130

Combination Therapy: Radiation + Chemo

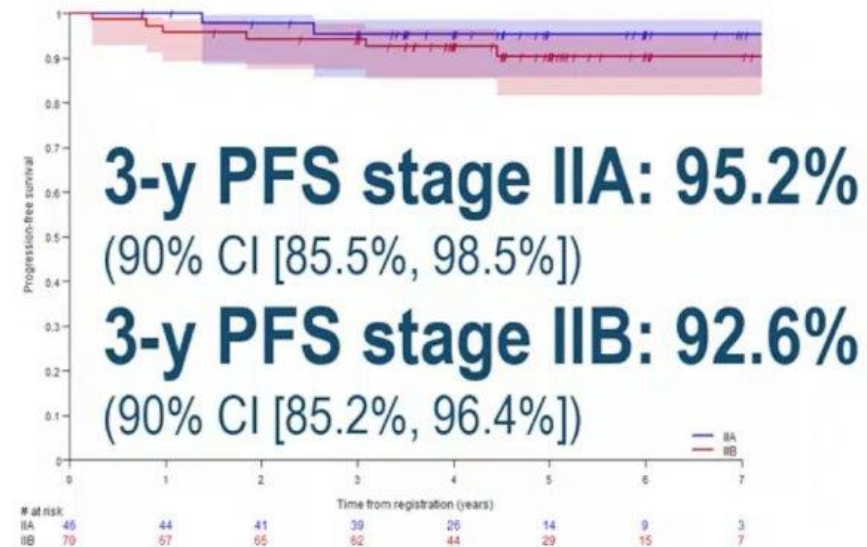
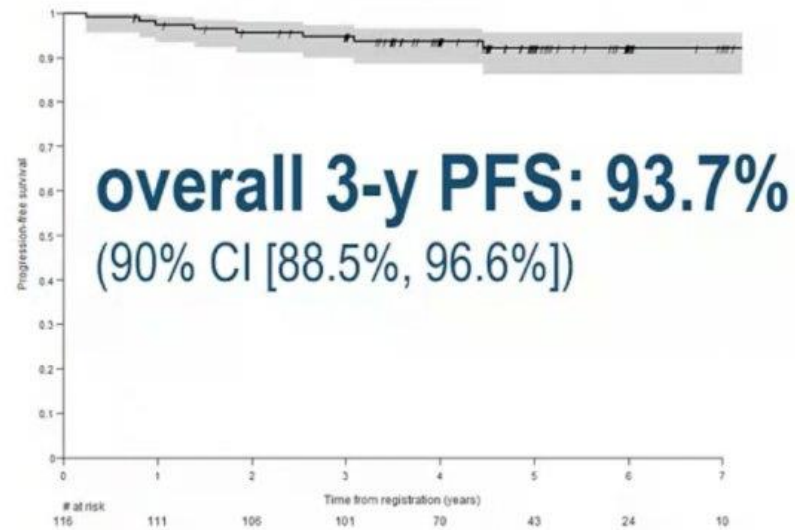
SAKK 01/10 – de-escalation of combined chemotherapy & radiation
Single arm Phase II trial, n=120



“Importantly, the median planned target volume was ~25% of a typical, standard of care dog-leg planned target volume, thus a 75% median decrease in irradiated volume.”

SAKK 01/10 Results

Median FU: 4.5 years



*Primary end point (3y PFS) not met – lower limit CI < 90%

Grade 3 or treatment related worse adverse events were mainly chemotherapy associated cytopenias (7%)

Conclusions

- Radiation has long been a mainstay of treatment for IIA/B seminomas
- Radiation, chemotherapy, and RPLND all have comparable efficacy and low short-term toxicity
- Long term concern for radiation is secondary malignancies
- Radiation toxicities can be mitigated with advanced techniques including proton therapy
- SAKK 01/10 demonstrated that low doses of radiation + chemotherapy exhibit promise, possibility of investigating other combinations (surgery + radiation?)



