



LEIDEN UNIVERSITY MEDICAL CENTER

**Sarcoma
Patients
EuroNet**

Unanswered questions and future research

**Rick Haas
Dept. of Radiotherapy
the Netherlands Cancer Institute – Amsterdam
the Leiden University Medical Center**

Disclosures

Investigator Initiated Research Grants from

GSK

Novartis

Nanobiotix Company

PharmaMar

but none of them had part in the design nor the conduct of my studies

Unanswered questions: to name a few...

What is the standard of care ?

What happens if you refrain from RT ?

What total dose ?

What RT fraction size ?

Presentation

NCIC-SR2 randomized trial and its implications for 50Gy

Possible alternatives

Presentation

NCIC-SR2 randomized trial and its implications for 50Gy

Possible alternatives

no RT

Presentation

NCIC-SR2 randomized trial and its implications for 50Gy

Possible alternatives

no RT

fraction size

total dose

overall treatment time

Presentation

NCIC-SR2 randomized trial and its implications for 50Gy

Possible alternatives

no RT

fraction size

total dose

overall treatment time

combined modality regimens

conventional chemotherapy

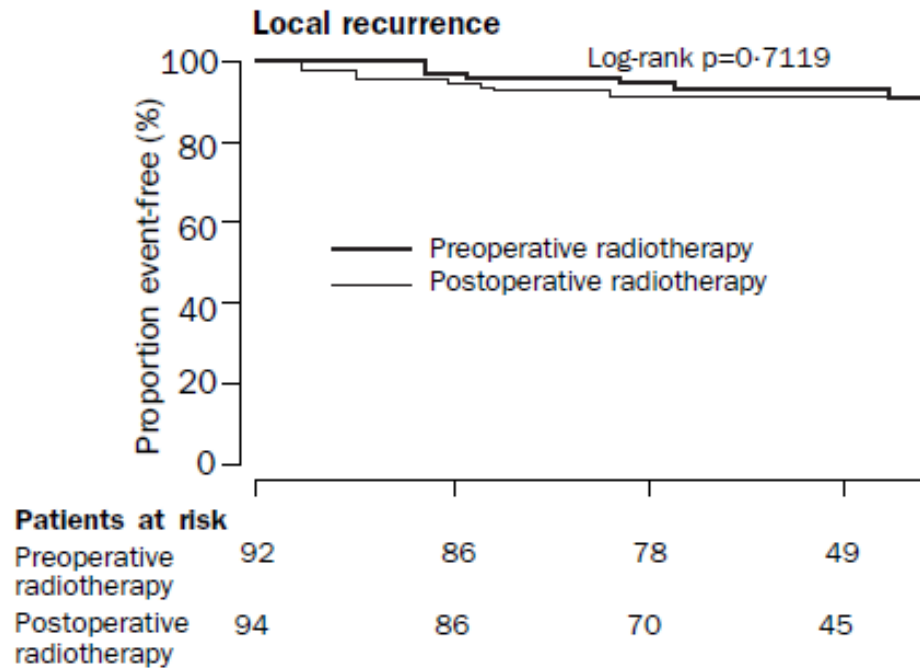
targeted agents

NCIC SR-2

Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomised trial

Brian O'Sullivan, Aileen M Davis, Robert Turcotte, Robert Bell, Charles Catton, Pierre Chabot, Jay Wunder, Rita Kandel, Karen Goddard, Anna Sadura, Joseph Pater, Benny Zee

Lancet 2002; pre- versus postop RT (50 Gy vs 66 Gy)



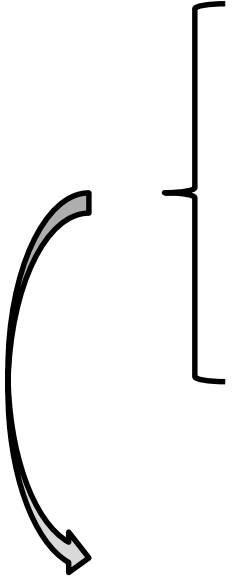
NCIC SR-2

Current standard (outside prospective clinical trials):

- 1.8-2 Gy per fraction**
- once-daily**
- 50-50.4Gy total dose**
- IMRT highly preferred for most cases**
- 5-6 weeks overall treatment time**

NCIC SR-2

Current standard (outside prospective clinical trials):

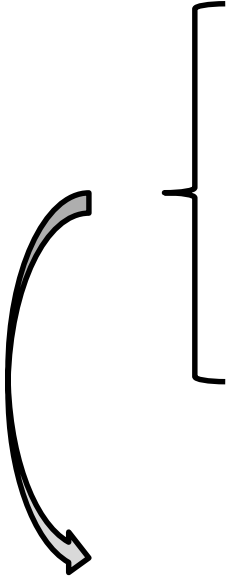


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“several” weeks delay / rest

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“several” weeks delay / rest



definitive surgery

NCIC SR-2

Balancing during MTD:

**wound complications vs late morbidity
&
local recurrence**



No RT

Does every ESTS patient need RT ?

No RT

Does every ESTS patient need RT ?

How large is the detrimental effect on local control when refraining from RT ?

No RT

Sources: the “no” RT arms of randomized trials
MSKCC prediction tool

No RT

the “no” RT arms of randomized trials

Randomized data on Surgery Alone and (neo-) adjuvant RT plus Surgery in ESTS			
Author	n	RT regimen	Local control (@ X years)
Pisters [1996]	164	0 Gy (surgery only)	69% @ 5 yrs
		42 – 46 Gy brachytherapy	82% @ 5 yrs
Yang [1998]	141	0 Gy (surgery only)	In high grade STS 78% versus 100% @ 10 yrs
		45 + 18 Gy postoperative	In low grade STS 68% versus 95% @ 10 yrs

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No RT

The MSKCC prediction tool

Memorial Sloan Kettering Cancer Center.

Prediction Tools ▶ Sarcoma Nomograms ▶ Local Recurrence Risk after Limb-Sparing Surgery without Radiation Nomogram

mskcc.org
PREDICTION TOOLS

▶ SARCOMA INFORMATION | ▶ MAKING AN APPOINTMENT

Sarcoma Nomogram: Local Recurrence Risk after Limb-Sparing Surgery without Radiation Nomogram

TEXT SIZE

This tool can be used to predict the chance of soft tissue sarcoma returning at the site of initial surgery after the tumor is removed through limb-sparing surgery if the patient does NOT receive radiation. The probability of local recurrence is calculated for both three years and five years after surgery.

Enter Your Information

Age

Tumor Size
Select the tumor size.

Margin
Select the tumor margin.

Grade
Select the tumor grade.

Histology
Select the histology.

Your Results


[Learn more](#) about your results below.

Probability of Local Recurrence	3 Year	
	5 Year	

Make an Appointment

Call us to schedule an appointment or contact us online

[Contact Us ▶](#)



No RT

The MSKCC prediction tool

Retrospective database

684 primary ESTS patients

treated by surgery alone

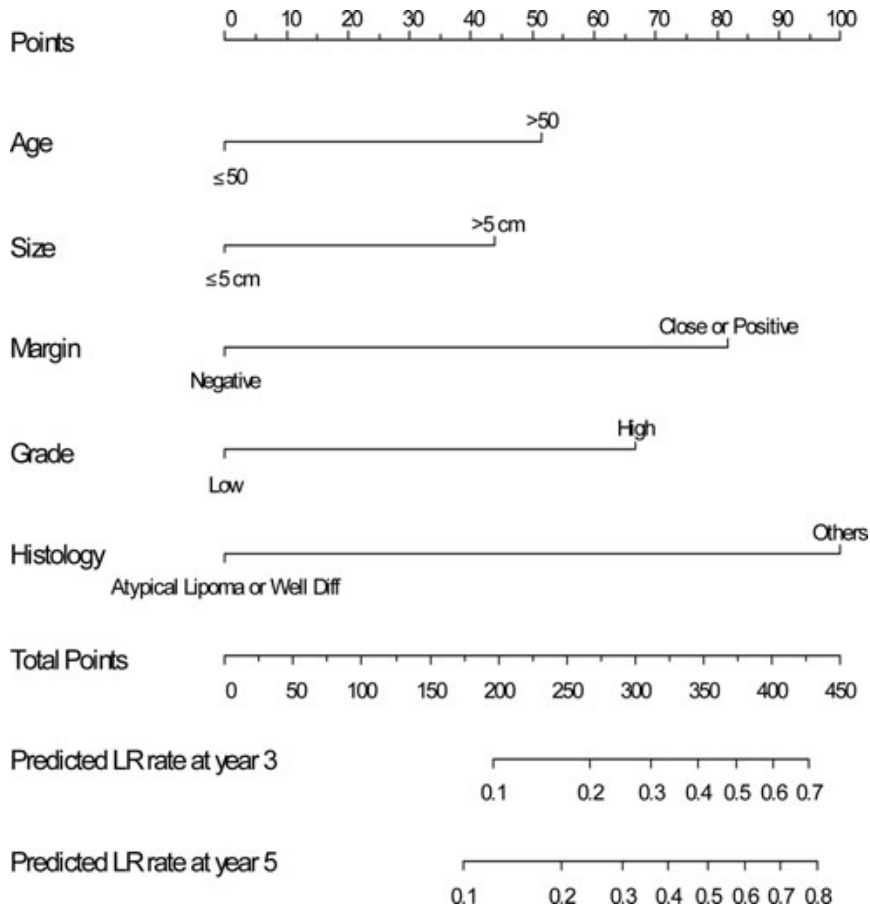
1982-2006, median FU 58 mos

ORIGINAL ARTICLE

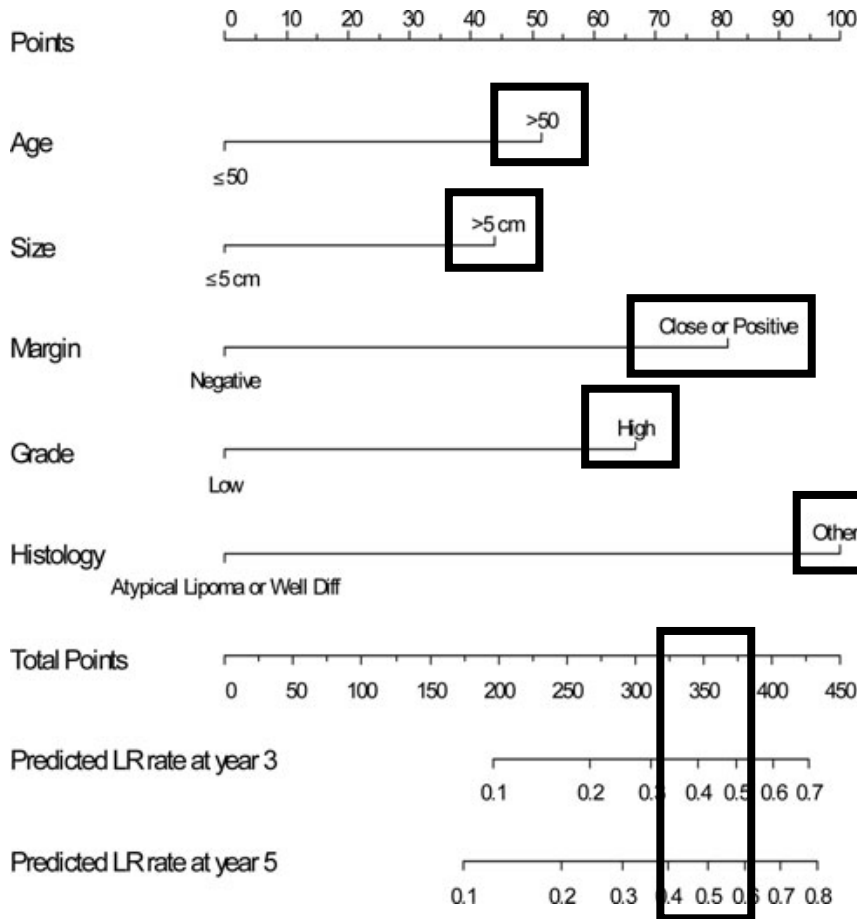
A Postoperative Nomogram for Local Recurrence Risk in Extremity Soft Tissue Sarcomas After Limb-Sparing Surgery Without Adjuvant Radiation

Oren Cahlon, MD, Murray F. Brennan, MD,† Xiaoyu Jia, MS,‡ Li-Xuan Qin, PhD,‡ Samuel Singer, MD,† and
Kaled M. Alektiar, MD**

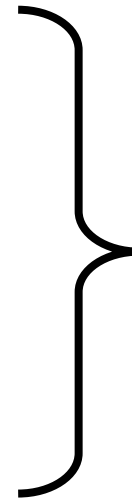
No RT



No RT



Elderly patient
large, deep seated UPS
marginal surgery



40-50% chance on LR

Fraction size, total dose and OTT

Fraction size, total dose and OTT

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1.8-2 Gy per fraction

once-daily

50-50.4Gy total dose

IMRT highly preferred for most cases

5-6 weeks overall treatment time

Fraction size, total dose and OTT

Alternatives

Fraction size, total dose and OTT

Preoperative RT in ESTS: altered fractionation.

Author	n	RT regimen	Local control (@ X years)
Eilber [1974 - 1981]	77	10 x 3.5 Gy	95% @ 8 yrs
Eilber [1981 - 1984]	137	5 x 3.5 Gy	88% @ 4 yrs
Eilber [1984 - 1987]	112	8 x 3.5 Gy	95% @ 2 yrs

Fraction size, total dose and OTT

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Temple [1997]	42	10 x 3 Gy	97% @ 5 yrs

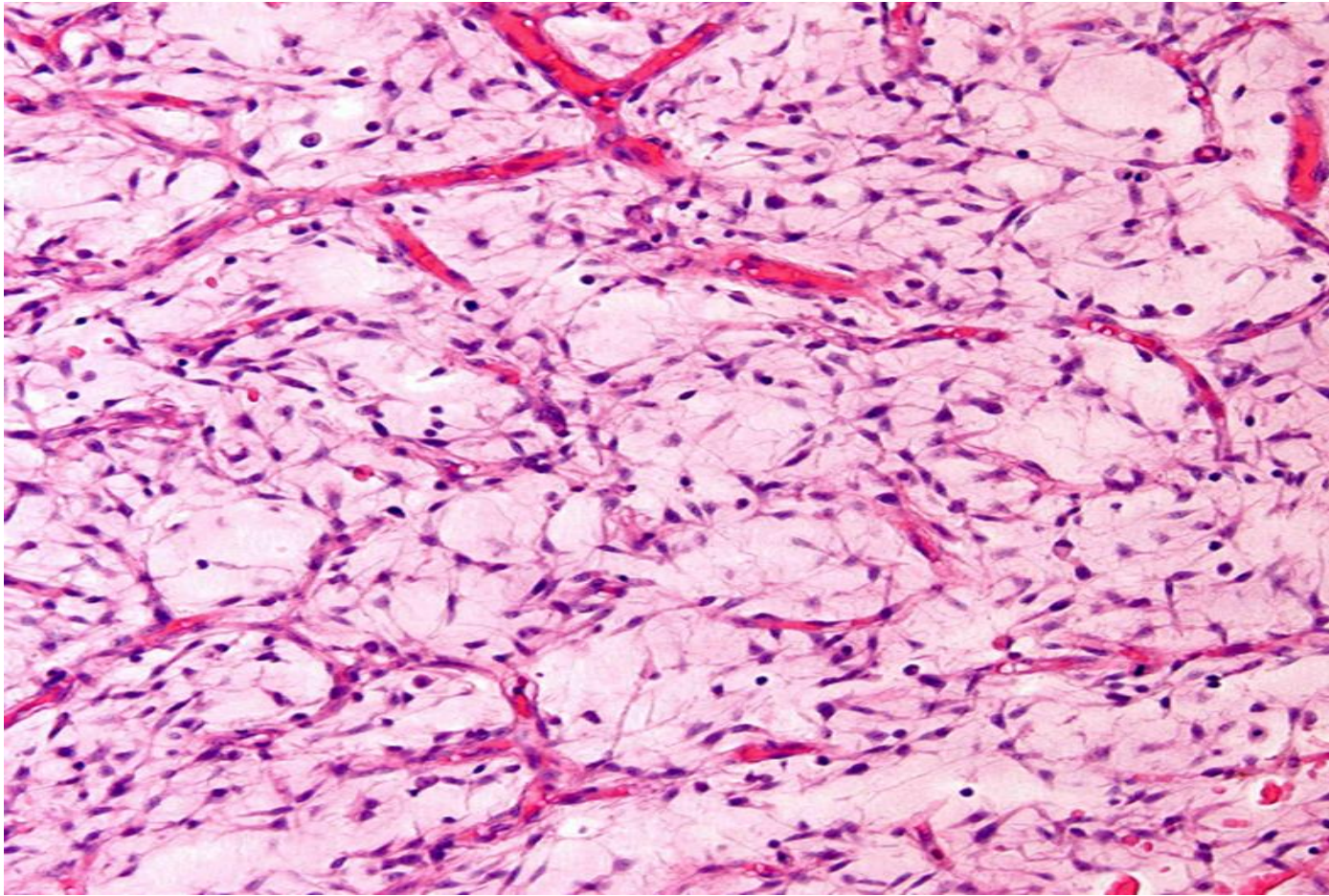
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Eilber [1984 - 1987]	112	8 x 3.5 Gy	95% @ 2 yrs
Temple [1997]	42	10 x 3 Gy	97% @ 5 yrs
Kosela [2014]	272	5 x 5 Gy	81% @ 3 yrs

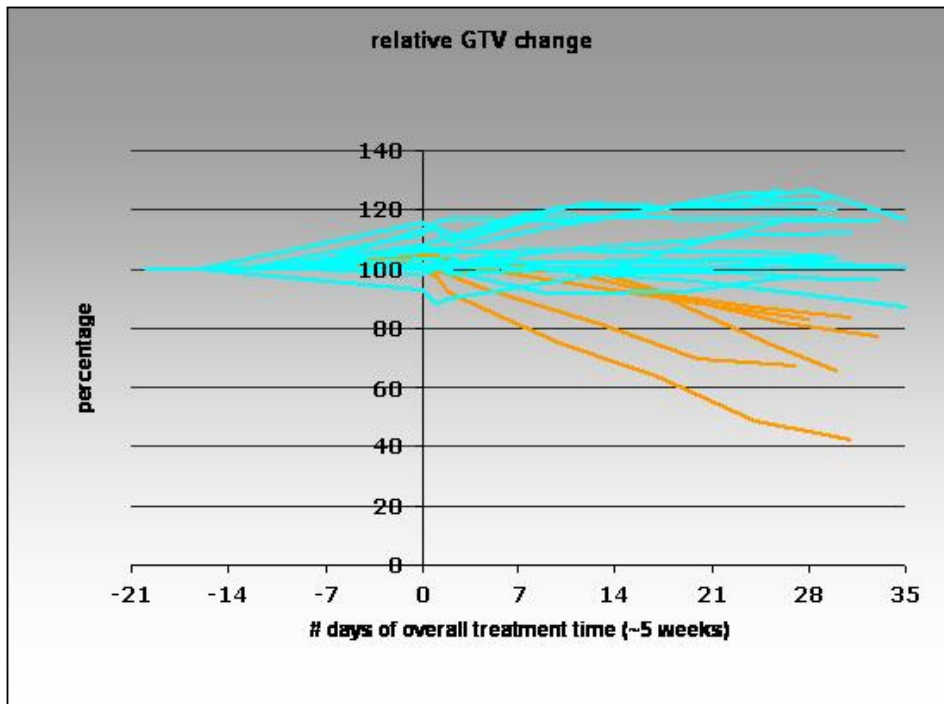
Fraction size, total dose and OTT

Myxoid liposarcomas



Fraction size, total dose and OTT

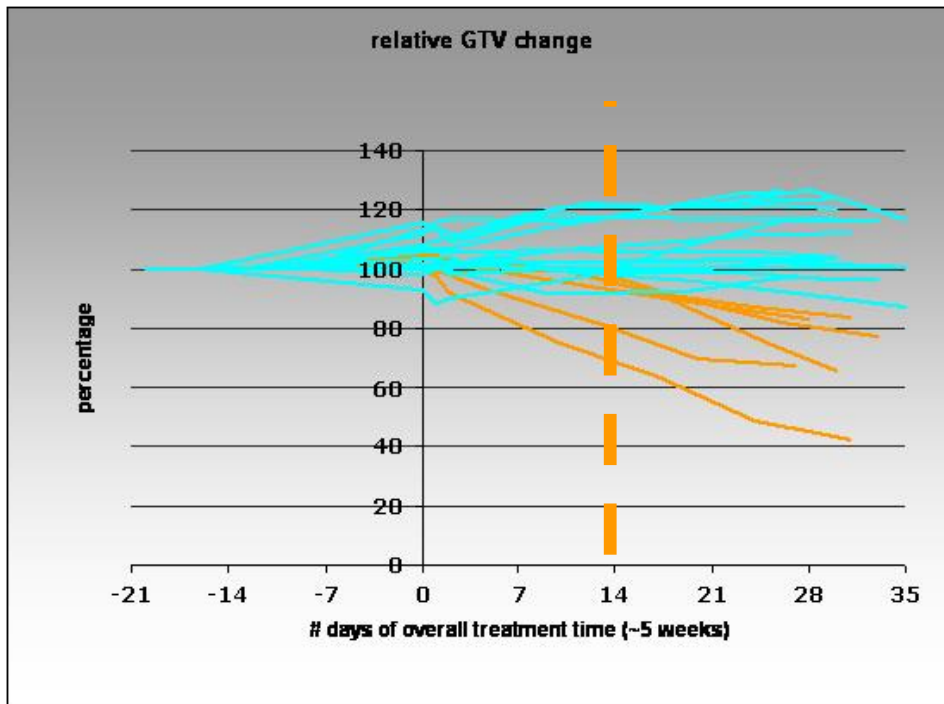
Myxoid liposarcomas: volume shrinkage as early event



Courtesy Anja Betgen MSc NKI-AvL

Fraction size, total dose and OTT

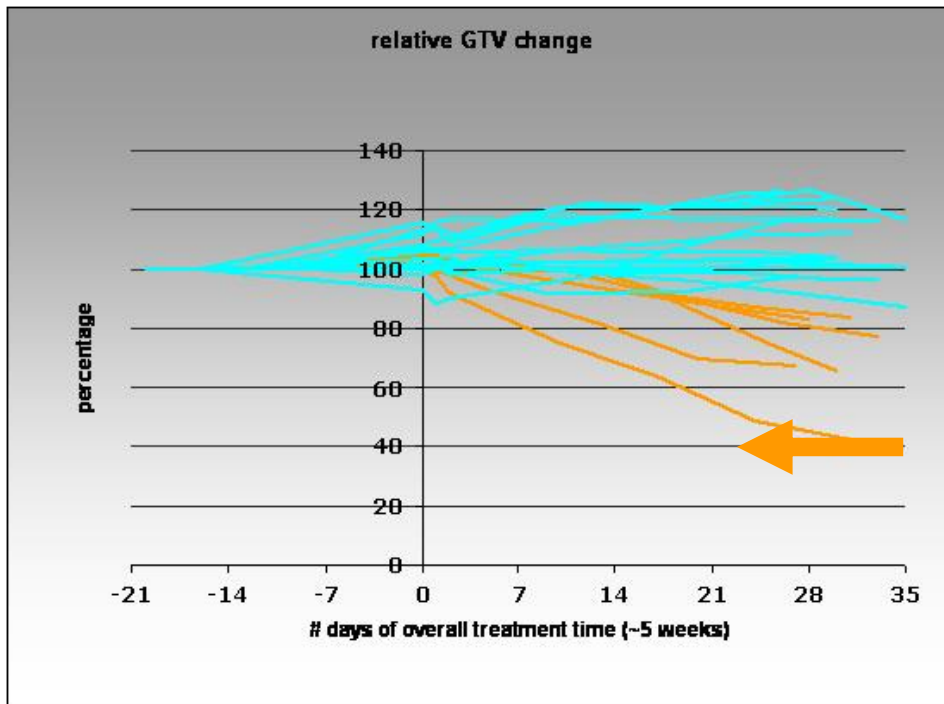
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Fraction size, total dose and OTT

Myxoid liposarcomas: opportunity for dose reduction ?



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Fraction size, total dose and OTT

Myxoid liposarcomas: opportunity for dose reduction ?

ClinicalTrials.gov

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[Home](#) > [Find Studies](#) > [Study Record Detail](#)

Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcomas (DOREMY)

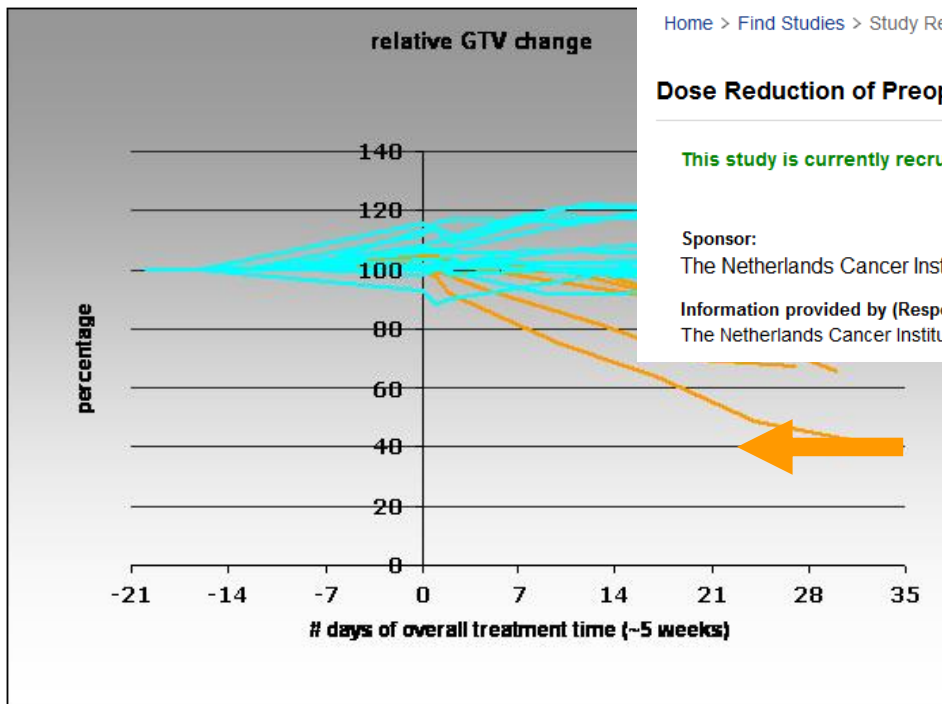
This study is currently recruiting participants. (see [Contacts and Locations](#))

Sponsor:
The Netherlands Cancer Institute

Information provided by (Responsible Party):
The Netherlands Cancer Institute

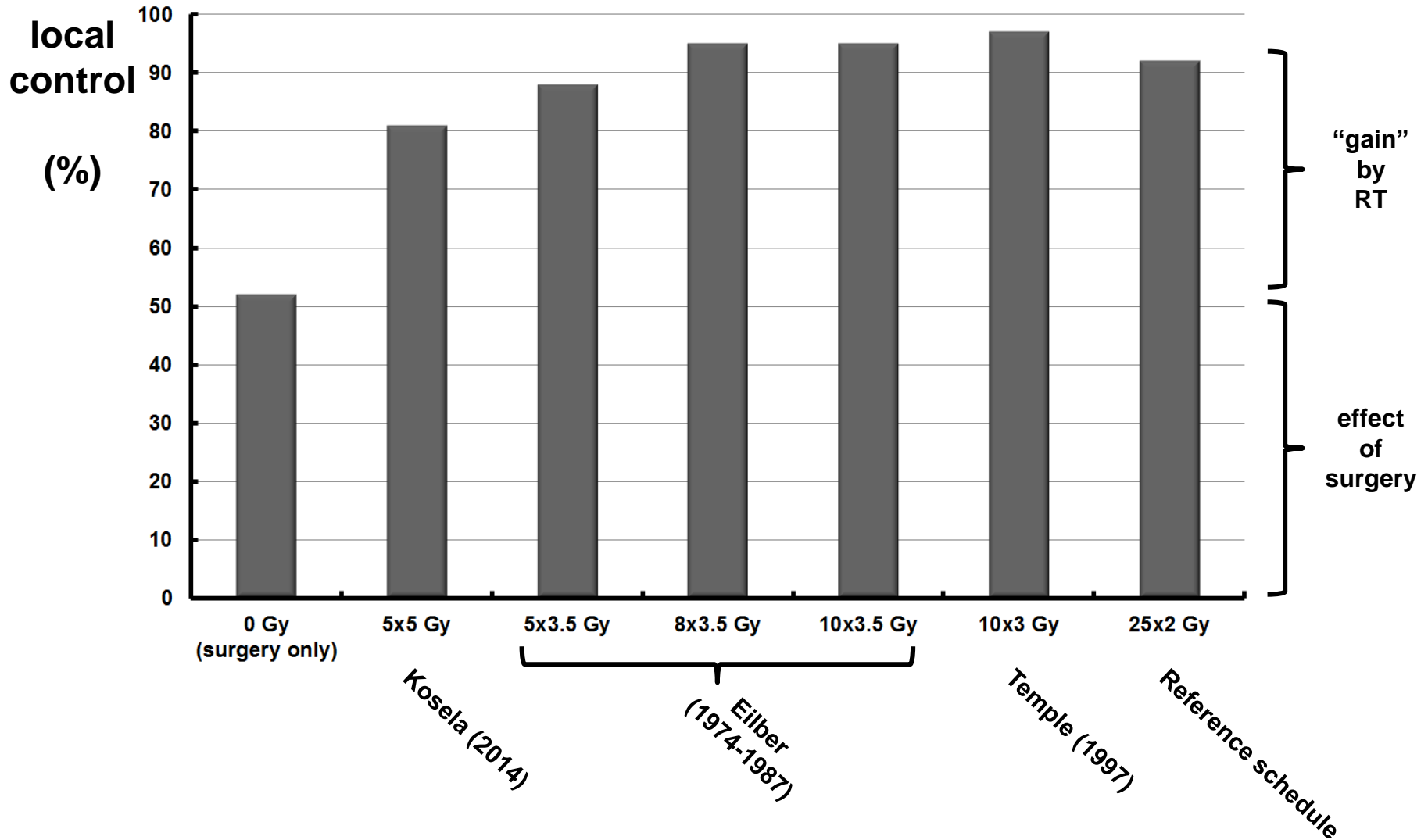
ClinicalTrials.gov Identifier:
NCT02106312

First received: March 6, 2014
Last updated: April 10, 2014
Last verified: November 2012
[History of Changes](#)



Courtesy Anja Betgen MSc NKI-AvL

Local control versus RT dose



Combined modality regimens

Preoperative RT in ESTS in combination with systemic therapy.

Setting	Author	n	RT regimen	CT regimen	(near) pCR	Local control (@ X years)
RT only	Canter	25	25 x 2 Gy	-	8%	100% @ 3 yrs
	Shah	30	25 x 2 Gy	-	10%	100% @ 5 yrs

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	Ryan	25	8 x 3.5 Gy	Adria / Ifos	40%	88% @ 2 yrs
	MacDermid	34	8 x 3.5 Gy	Ifos	11.8%	89% @ 5 yrs

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RT + targeted agents	Yoon	20	28 x 1.8 Gy	Avastin	20%	95% @ 2 yrs
	Canter	8	25 x 2 Gy	Sorafenib	38%	100% @ 3 yrs
	Meyer	16	8 x 3.5 Gy	Sorafenib	44%	100% @ 2 yrs
	Lewin	9	28 x 1.8 Gy	Sunitinib	–	–
	Haas	11	25 x 2 Gy	Pazopanib	40%	91% @ 2 yrs

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RT + intratumoral nanoparticles	Bonvalot	20	25 x 2 Gy	Hafnium oxide nanoparticles	18%	–

In Conclusion



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Unanswered questions and future research

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In Conclusion

In case preoperative RT is preferred



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Questions for future research

fraction size

total dose

combined modality regimens





LEIDEN UNIVERSITY MEDICAL CENTER

Unanswered questions and future research

**Thanks for the invitation &
Thanks for your attention**

Rick Haas



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