

Post ESMO/WCLC 2017:

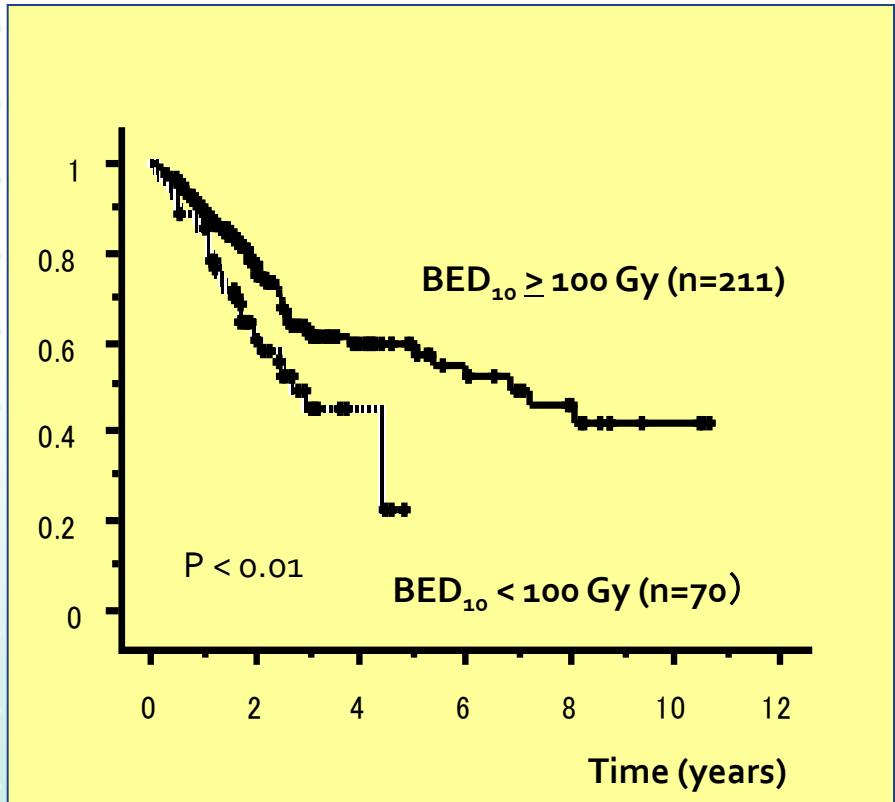
Radiotherapie

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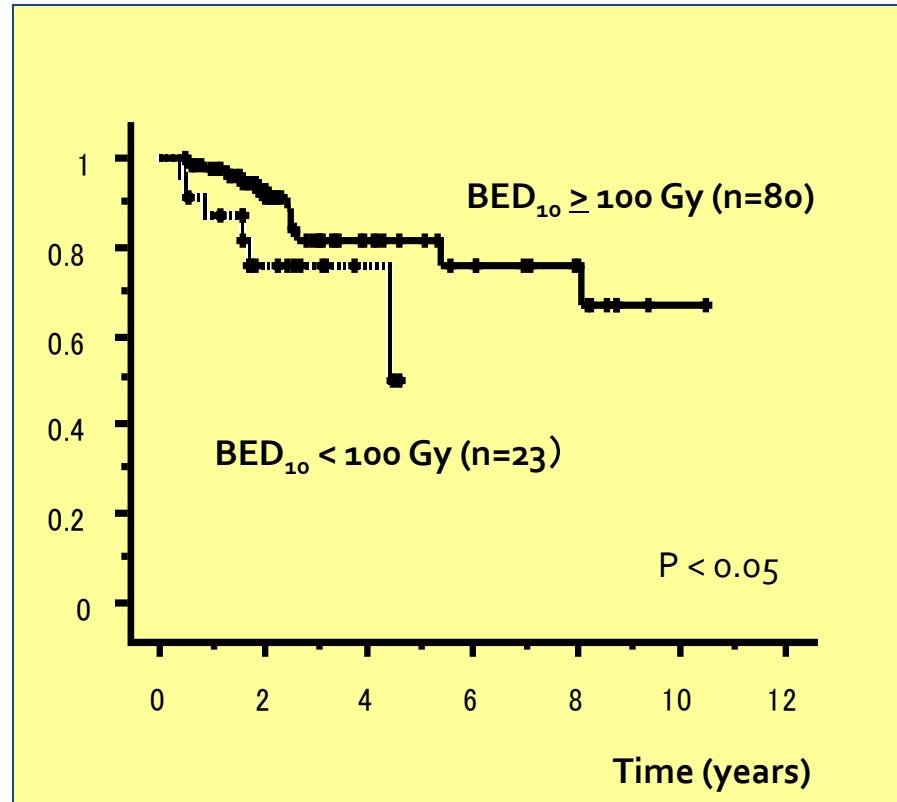
Conflict of Interest

- None to declare

Overall survival $BED_{10} < 100$ vs. $BED_{10} \geq 100$



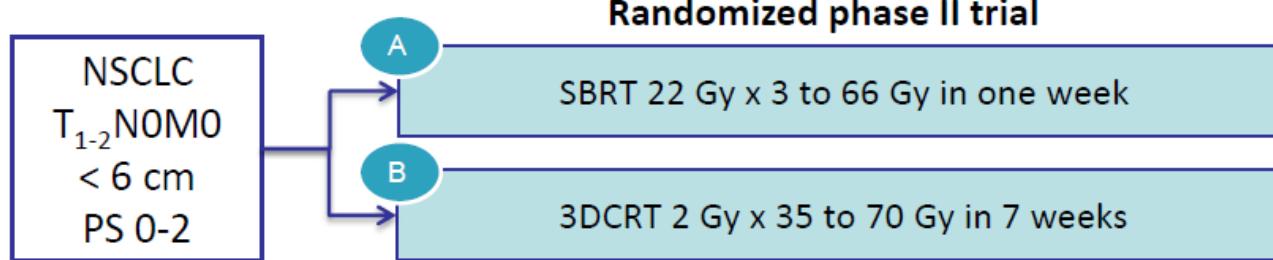
Overall survival in all patients



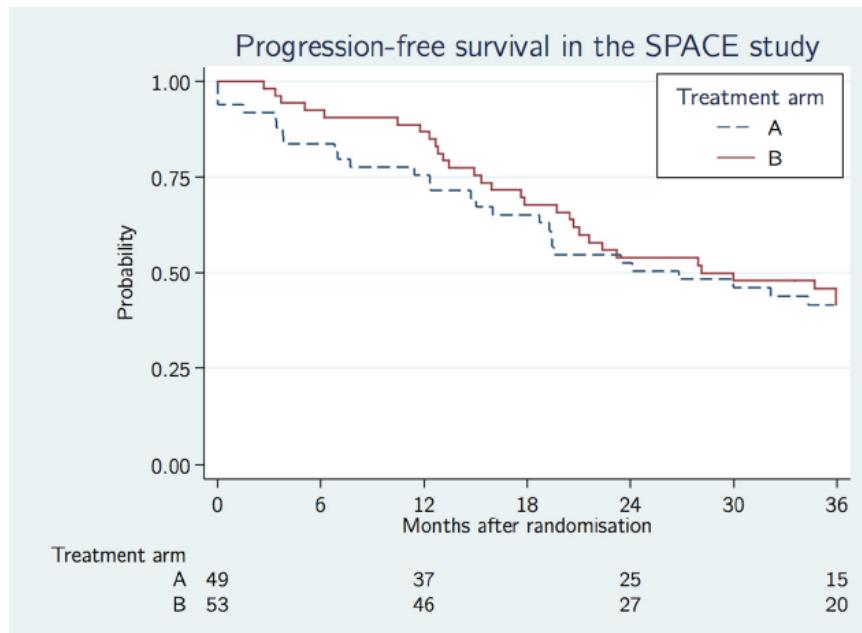
Overall survival in operable patients

SPACE study

$3 \times 15 \text{ Gy on the PTV edge}$
 $= 103 \text{ Gy EQD}_{2,T} (\text{a/b}=8 \text{ Gy})$



Primair eindpunt:
PFS



$= 58 \text{ Gy EQD}_{2,T} (\text{a/b}=8 \text{ Gy})$

Fig. 1. Progression free survival by treatment arm (A = SBRT, B = 3DCRT), ITT analysis. HR = 0.85, 95% CI: 0.52–1.36.

CHISEL: A randomized phase III trial of SABR vs conventional radiotherapy for inoperable stage I non-small cell lung cancer

TROG 09.02, ALTG 09.05

Trial Registration NCT01014130

David Ball, Tao Mai, Shalini Vinod, Scott Babington, Jeremy Ruben, Tomas Kron,
Brent Chesson, Alan Herschtal, Marijana Vanevski, Angela Rezo, Christine
Elder, Marketa Skala, Andrew Wirth, Greg Wheeler, Adeline Lim, Mark Shaw
On behalf of the CHISEL investigators



CHISEL Aims

Hypothesis:

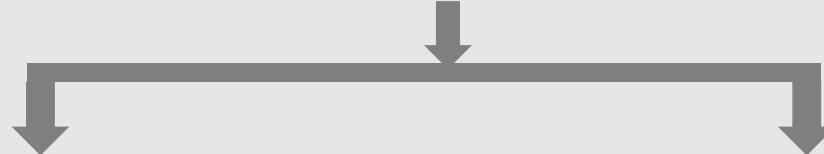
- SABR with a hypofractionated dose of 54 Gy in 3 fractions or 48 Gy in 4 fractions results in superior local control of peripherally located inoperable T₁–T_{2a} No non-small cell lung cancer compared with more fractionated conventional radiotherapy (66 Gy in 33 fractions or 50 Gy in 20 fractions)

Endpoints:

- Primary: - Time to local failure
- Secondary: - Overall and lung cancer specific survival
 - Toxicities (CTCAE v 4.0)
 - Quality of life (QLQ C30 and LC 13, State-Trait Anxiety Inventory)

Study design

Stratify:
T1 vs T2a
Medically inoperable vs medically operable
Randomize 2:1



54 Gy 3 fx in 2 weeks
or
48 Gy 4 fx in 2 weeks

66 Gy 33 fx in 6.5 weeks
or
50 Gy 20 fx in 4 weeks

140 Gy EQD_{2T}

96 Gy EQD_{2T}

56 Gy EQD_{2T}

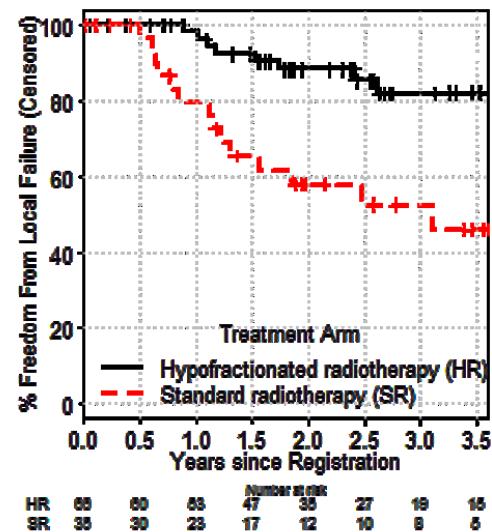
53 Gy EQD_{2T}

Patient characteristics (n =101)

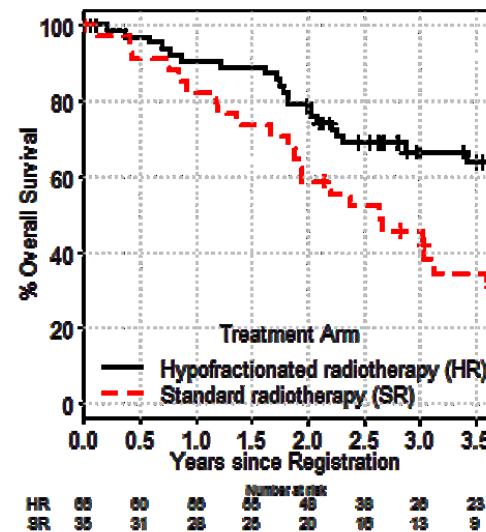
Characteristic	SABR (n=66)	CRT (n= 35)
Male sex	55%	57%
Median age (years)	73	77
Ever smoker	97%	100%
T1 stage	71%	69%
Comorbidity (median, range)	9 (6-19)	9 (0-17)
Maximum diameter (mm) (median, IQR)	22.5 19-31	27 20.5-32
Prior cancer	43%	31%



Freedom from local failure and overall survival



HR 0.29,
95% CI 0.13, 0.66
P = 0.002



HR 0.51
95% CI 0.29, 0.91
P = 0.020



Grade 3+ toxicities by arm

	SABR	Conventional
Dyspnoea	2 (1 grade 4)	0
Cough	2	0
Fatigue	1	0
Chest wall pain/pain	1	2
Lung infection	1	0
Hypoxia	1	0
Weight loss	1	0

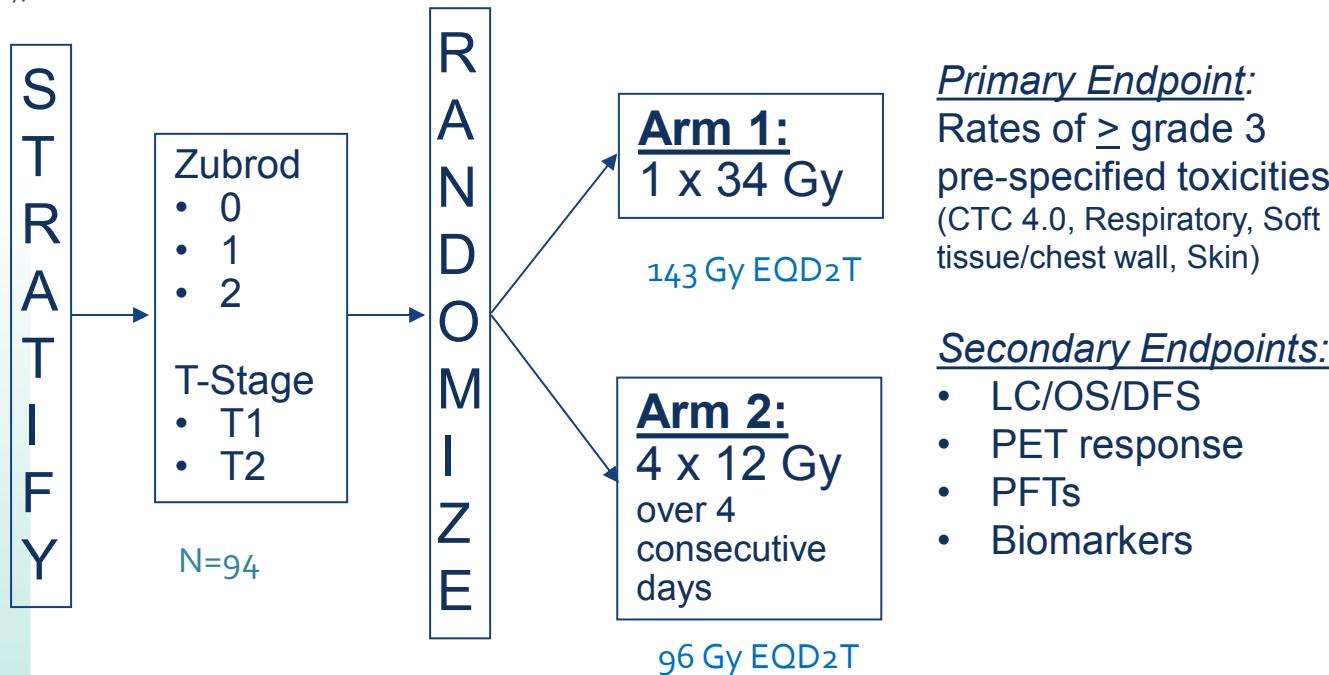


Conclusies voor ons

Niets veranderen

Long term follow-up on NRG Oncology RTOG 0915 (NCCTG No927): A randomized phase II study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer

Gregory M M Videtic, MD, Rebecca Paulus, BS, Anurag K Singh, MD, Joe Y Chang, MD, William Parker, MSc, Kenneth R Olivier, MD, Robert D Timmerman, MD, Ritsuko R Komaki, MD, James J Urbanic, MD, Kevin L Stephan, MD, Sue S Yom, MD, Clifford G Robinson, MD, Chandra P Belani, MD, Puneeth Iyengar, MD, Munther I Ajlouni, MD, Darindra D Gopaul, MD, Shashikant B Lele, MD, Ronald C McGarry, MD, Hak Choy, MD, Jeffrey D Bradley, MD



	<u>34 Gy/ 1 fr</u>	<u>48 Gy/ 4 fr</u>
N	41	45
LR	7.9 %	6.8 %
psAEs	10.3 %	13.3 %
PFS	19.1 Mo	31.8 Mo
Sec. prim.	15.5 %	13.3 %
5 y OS	28.8 %	40.2 %

Conclusies voor ons

- Nog preliminair
- Grote studies nodig
- 1 fractie: evolutie om te volgen

Toxicity and second primary lung cancers in late survivors following lung SBRT. Giuliani et al.

Second primaries:

2-4 %/year up to 18 years following treatment

- 1192 patients
- 5 y OS: 14 % (182 patients)
- *Toxicity*
 - G2 fatigue: 5/182 (2.7 %)
 - G2 rib fracture: 1/182
 - G2 chronic myositis: 8/182 (4.4 %)
- *Failures*
 - LR: 3/182; regional failure: 2/182; DM: 5/182
- *Second primary lung cancers*
 - 22 (12 %)

Conclusies voor ons

- Levenslang jaarlijks low-dose CT thorax?

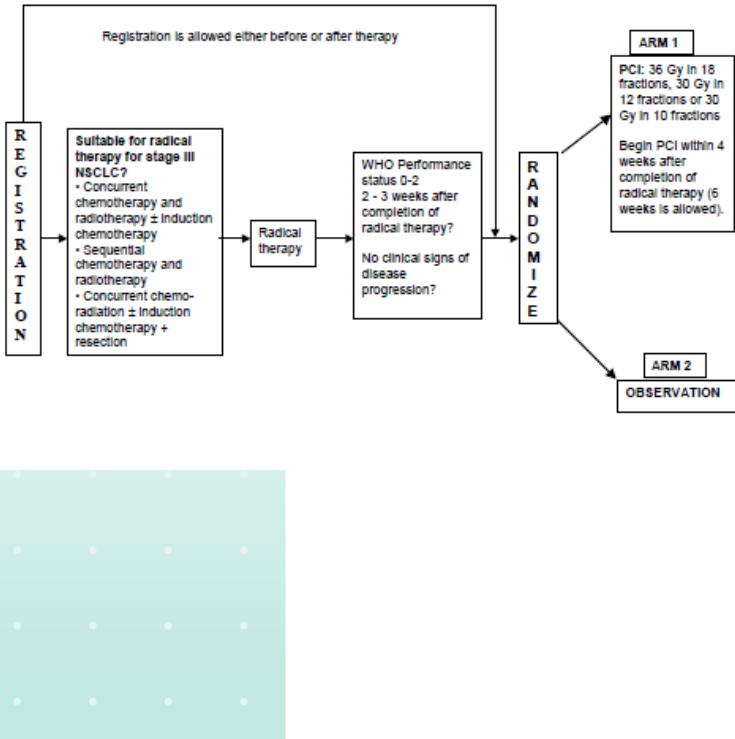
Toxicity results from the randomized phase III NVALT-11/ DLCRG02 study of prophylactic cranial irradiation vs. observation in stage III NSCLC

- De Ruysscher DKM (1), Dingemans A (1), Praag J (2), Belderbos J (3), C. Tissing-Tan C (4), Herder G (5), Haitjema T (6); Ubbels F (7); Lagerwaard J (8); Stigt J (9); Smit E (10); van Tinteren H (10), van der Noort V (10), Groen HJM (7)

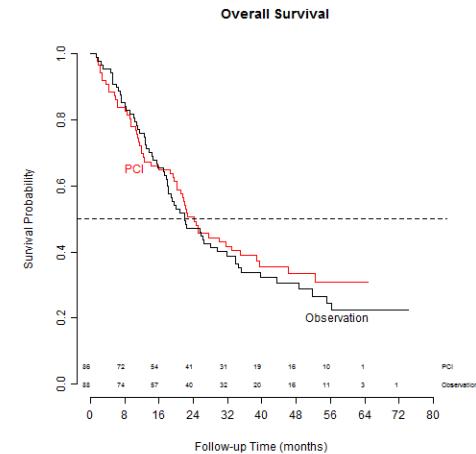
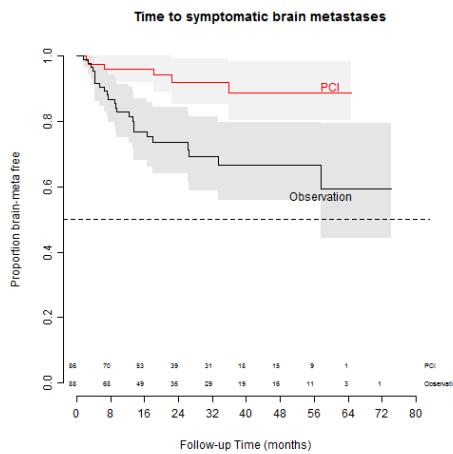
1 University Medical Center Maastricht and Maastro Clinic, Maastricht; 2 Erasmus Medical Center, Rotterdam; 3 Antonie van Leeuwenhoek hospital, Amsterdam; 4 Radiotherapeutic Institute Arnhem; 5 Antonius hospital Nieuwegein; 6 Medical Center Alkmaar; 7 University Medical Center Groningen; 8 Free University Medical Center, Amsterdam;
9 Isala hospital, Zwolle; 10 Netherlands Cancer Institute, Amsterdam; All in The Netherlands



Primary endpoint: Incidence of symptomatic brain metastases



	PCI (n=86)	Observation (n=88)	p
BM + neuro symptoms	6 (7.0 %)	24 (27.2 %)	< 0.001



All neurological adverse events: Physician rated

	All grades		Grade 3, 4, 5	
	PCI	Observation	PCI	Obs
Memory impairment	86	88	86	88
Cognitive disturbance	26	7	0	0
	18	3	2	0

After Holms-Bonferoni correction: significant differences between arms considering all grades: **Memory impairment and cognitive disturbance.**

Grade 3-5: number of AE too small to see significant differences.

All non-neurological adverse events Physician rated

	All grades		Grade 3, 4, 5	
	PCI	Observation	PCI	Obs
Alopecia	86	88	86	88
Fatigue	36	5	0	0
Headache	55	30	13	2
	19	1	0	0

After Holms-Bonferoni correction: significant differences between arms considering all grades: **Alopecia, fatigue, headache**

Grade 3-5: number of AE too small to see significant differences.

Patient reported adverse events

	All grades		Grade 3, 4	
	PCI	Observation	PCI	Obs
	86	88	86	88
Dizziness	50	36	1	0
Headache	55	36	4	2
Fatigue	69	70	3	5
Memory impairment	50	47	2	1
Vomiting	16	6	0	0

After Holms-Bonferoni correction: significant differences between arms considering all grades: **headache**

Grade 3-5: number of AE too small to see significant differences.

Conclusions/ Take home messages

- PCI reduces *symptomatic* brain metastases (7 % vs. 27 %), but at the expense of increased side effects
- When rated by physicians, G1-2 cognitive disturbance (3.4 % vs. 20.9 %) and G1-2 memory impairment (7.9 % vs. 30.2 %) are significantly increased
- Rated by patients, only headache G1-2 (40.9 % vs. 63.2 %) is significantly increased

- Detailed analysis of QoL is ongoing
- Strategies to reduce the toxicity of PCI (an efficient treatment) is needed (hippocampus sparing?)

