Combined modality lung cancer

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Conflict of Interest

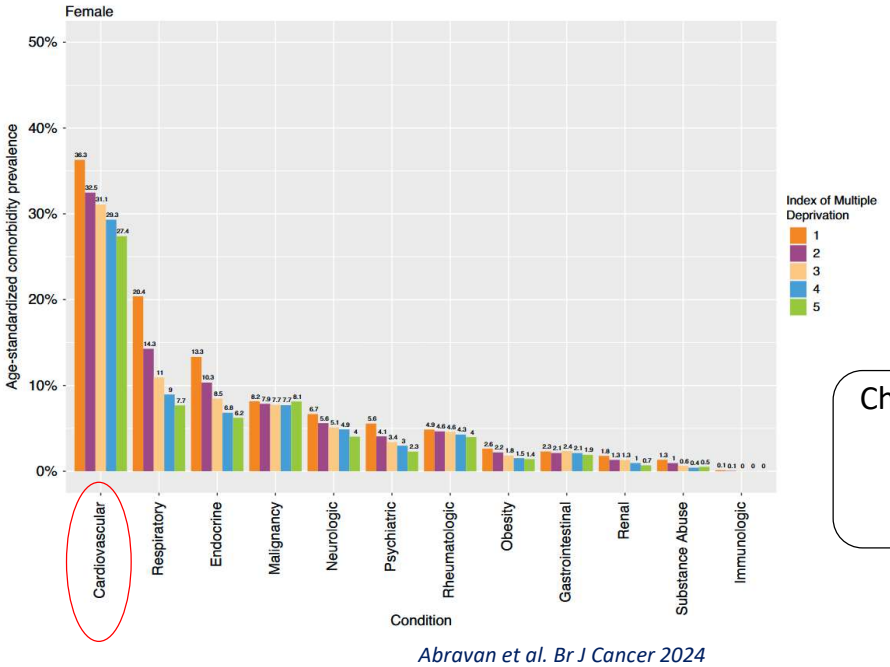
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- Research grant/ support: Bristol-Myers Squibb, AstraZeneca, Beigene, Philips, Olink, Pfizer
- Advisory board: Bristol-Myers Squibb, AstraZeneca, Philips, Eli-Lilly

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Patients with lung cancer are highly comorbid



Challenges with tolerance of side effects of drug-RT combinations
in a frail population

Abravan et al. Br J Cancer 2024

Not all (cardiac) events after radiotherapy are due to radiotherapy: Lung-ART

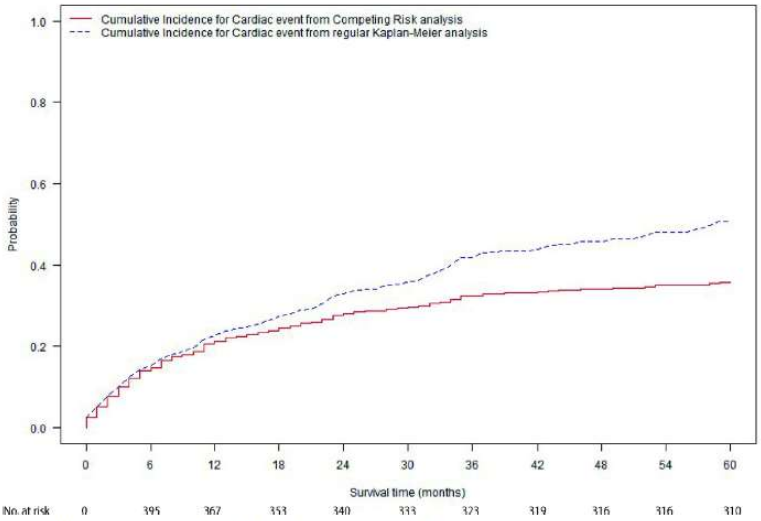
Total received dose (in Gy)†	
≤50	7/241 (3%)
51–57	231/241 (96%)
>57	3 (1%)
Main radiotherapy variables†	
Lung V20	23% (17–27)
Mean lung dose (Gy)	13 (10–15)
Mean heart dose (Gy)	13 (8–19)
Heart V35	15% (8–24)
PORT technique†	
Three-dimensional conformal radiotherapy	201/226 (89%)
Intensity-modulated radiotherapy	25/226 (11%)
Missing information	15

	PORT group (n=241)	Control group (n=246)	Difference
Deaths*	99 (41%)	102 (42%)	
Progression of recurrence	68 (69%)	87 (85%)	
Chemotherapy toxicity	1 (1%)	..	
Radiotherapy toxicity	2 (2%)	..	
Cardiopulmonary disease	16 (16%)	2 (2%)	
Second primary cancer	5 (5%)	1 (1%)	
Pulmonary infection	1 (1%)	..	
Vascular	1 (1%)	1 (1%)	
Other†	..	3 (3%)	
Unknown	5 (5%)	8 (8%)	
Adverse event, any grade‡	222 (92%)	200 (81%)	11 %
Early adverse events	215 (89%)	183 (74%)	15 %
Late adverse events	188 (78%)	153 (62%)	16 %
Adverse events, grade 3–5	60 (25%)	37 (15%)	10 %
Adverse events, grade 3 or 4	57 (24%)	37 (15%)	9 %
Early adverse events	28 (12%)	19 (8%)	
Late adverse events§	36 (15%)	22 (9%)	
Total late cardiac events	10 (4%)	5 (2%)	2 %
Cardiac ischaemia or infarction	3 (1%)	..	
Total late thoracic events	28 (12%)	9 (4%)	
Dyspnoea (thoracic)	7 (3%)	5 (2%)	1 %
Pneumonitis (thoracic)	9 (4%)	..	

Maastro *Le Pechoux et al. Lancet Oncol 2022*

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Most cardiac events occur within 1 year after radiotherapy



Cumulative incidence corrected for the competing risk of death.

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Degens, De Ruysscher, et al. BMJ Open 2020

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The region of the heart matters

Manchester patients | RTOG 0617 trial | PET-plan trial

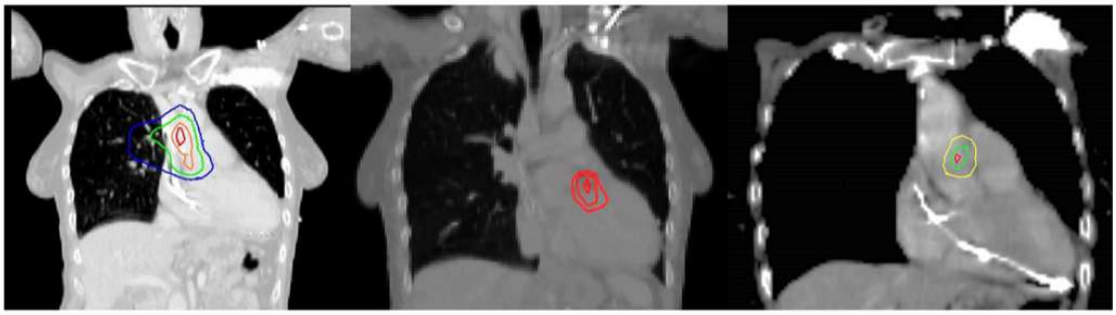


Figure 1. Dose-sensitive cardiac subregions found on image-based data-mining from retrospective study of patients treated at The Christie, RTOG 0617 trial, and PET-plan trial.

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Banfill et al. JTO Clin Res Rep 2024

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Dose matters

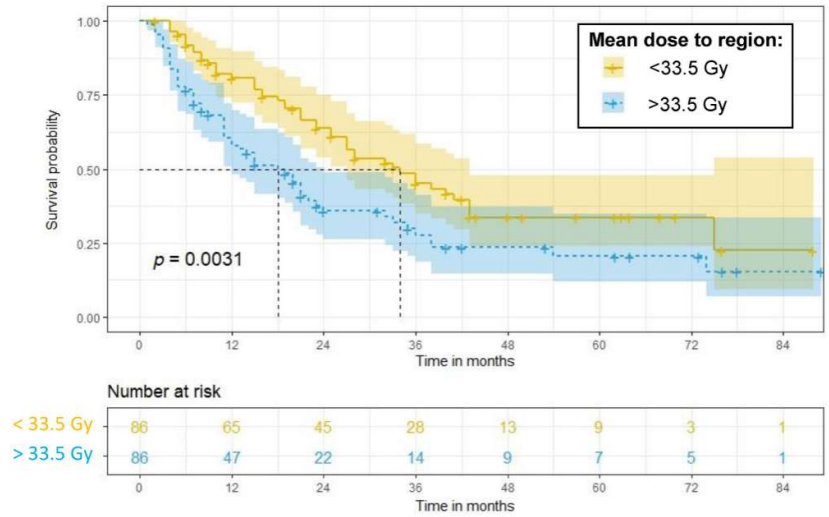


Figure 3. Kaplan-Meier survival curve split on median dose to the identified dose-sensitive region in the base of the heart.

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Craddock et al. JTO 2023

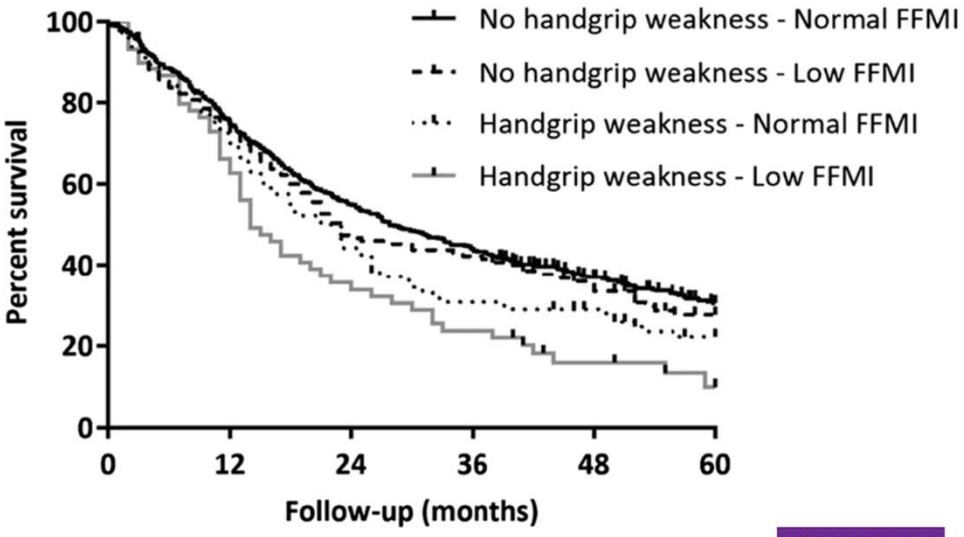
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Prognostic value of FFMI and handgrip strength NSCLC

N = 936

FFMI: Fat Free Mass Index

$$FFMI = \frac{FFM}{height\ (m)^2}$$

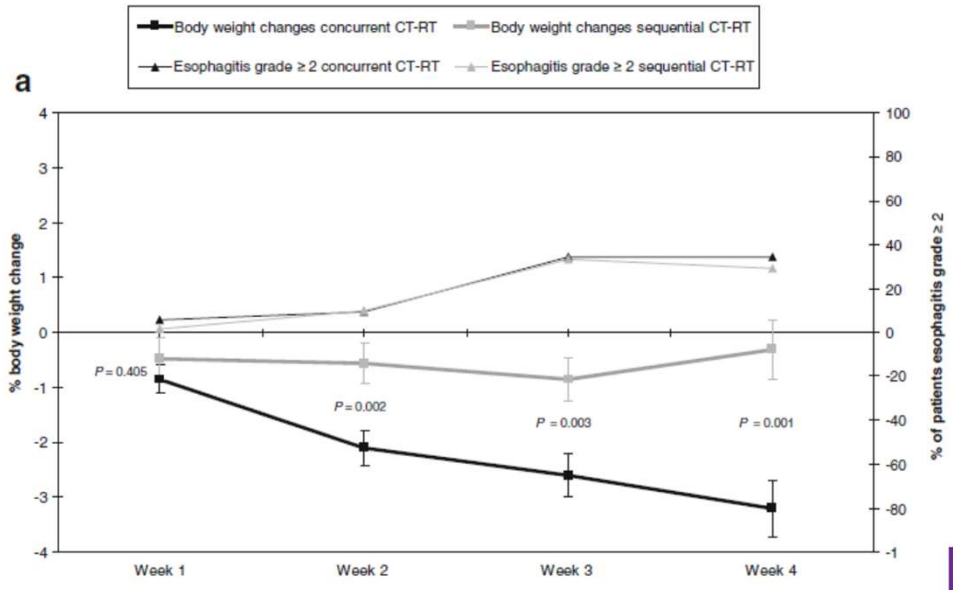


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Burtin, … De Ruysscher. J Cachexia Sarcopenia Muscle 2020

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Early weight loss during chemo-radiotherapy for stage III NSCLC is independent of esophagitis



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Op den Kamp C et al. J Cachexia Sarcopenia Muscle 2014

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nature cancer

Article

https://doi.org/10.1038/s43018-026-01161-y

Nivolumab plus chemoradiotherapy followed by nivolumab with or without ipilimumab for untreated locally advanced stage III NSCLC: a randomized phase 3 trial

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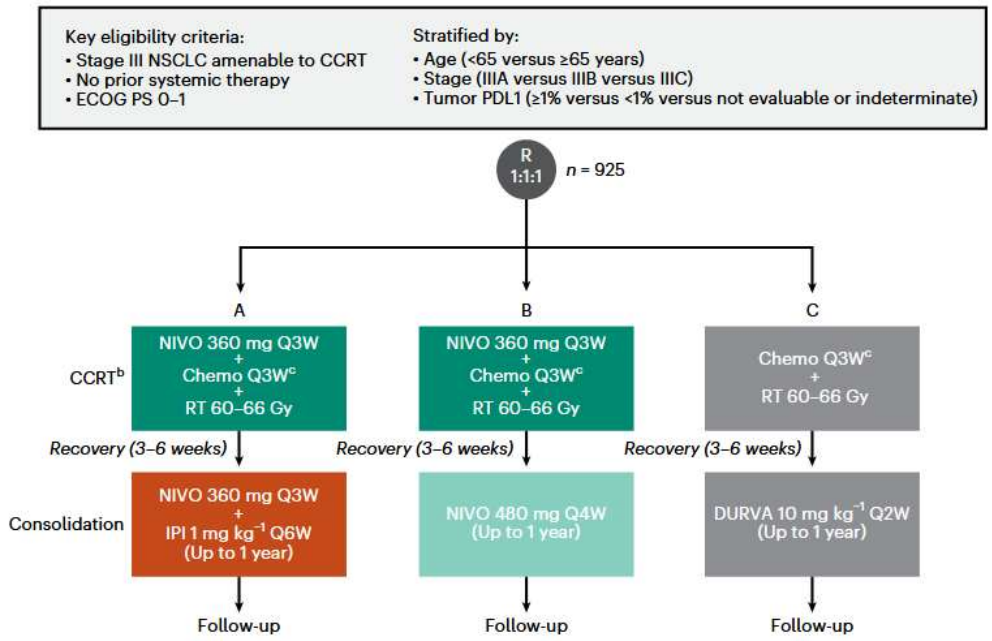
Check for updates

Solange Peters[1], Daniel S. W. Tan[2,3], David E. Gerber[4], James Urbanic[5], Suresh Ramalingam[6], Jinming Yu[7], Ligang Xing[7], Achim Rittmeyer[8], Tudor-Eliade Ciuleanu[9], Juliana de Menezes[10], Hye Ryun Kim[11], Carlos Rojas[12], Konstantinos Syrigos[13], Hidetoshi Hayashi[14], Anoop Haridass[15], Diego Cortinovis[16,17], Debora Bruno[18], Martin Kimmich[19], Antonio Calles[20], Raheel Nathani[21], Geetha Pudussery[21], Luoying Yang[21] & Dirk De Ruysscher[22]

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Peters et al. Nature Cancer 2026

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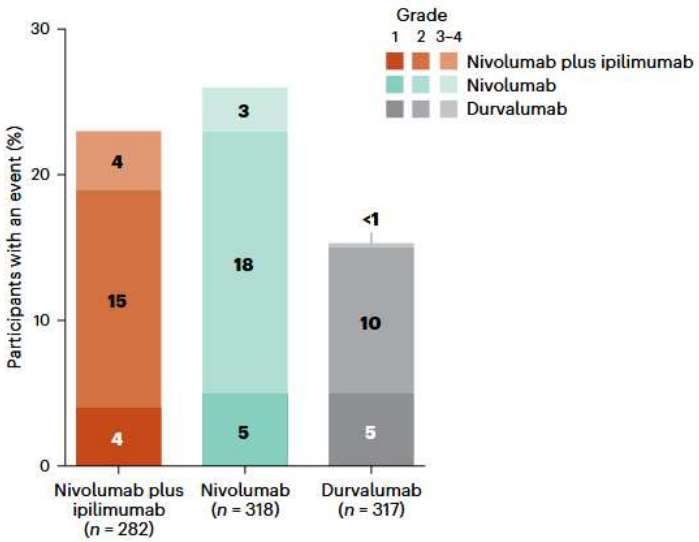


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Peters et al. Nature Cancer 2026

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Pneumonitis per treatment arm



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Peters et al. Nature Cancer 2026

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Conclusions

- Awareness of complex drug–radiotherapy interactions is essential, with the sequence of administration playing a critical role
- Optimal combinations may also impact (occult) distant metastatic disease, beyond local control
- Treatment combinations must remain tolerable, particularly given the high burden of co-morbidities in this population
- Pneumonitis remains an important dose-limiting toxicity ➔ consider biological optimized doses
- High prevalence of sarcopenia and cachexia ➔ novel approaches are increasingly needed and emerging
- Oesophagitis may be dose-limiting ➔should be carefully anticipated and mitigated
- There is currently no reliable surrogate for predicting late toxicities
- Need biomarkers

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