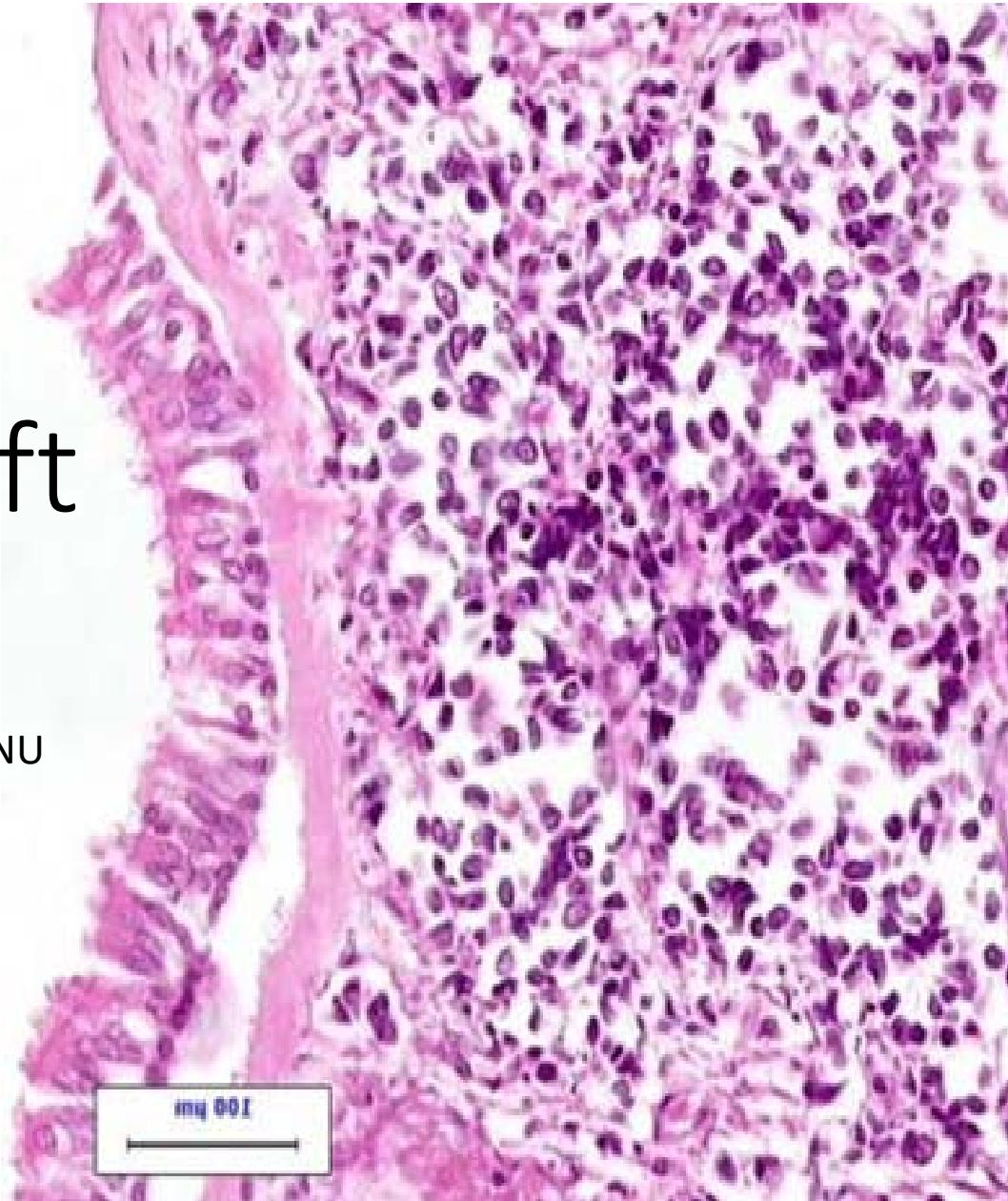


# Immunterapi ved småcellet lungekreft

Bjørn H. Grønberg

Professor, Institutt for klinisk og molekylær medisin, NTNU

Overlege, Kreftklinikken, St. Olavs hospital

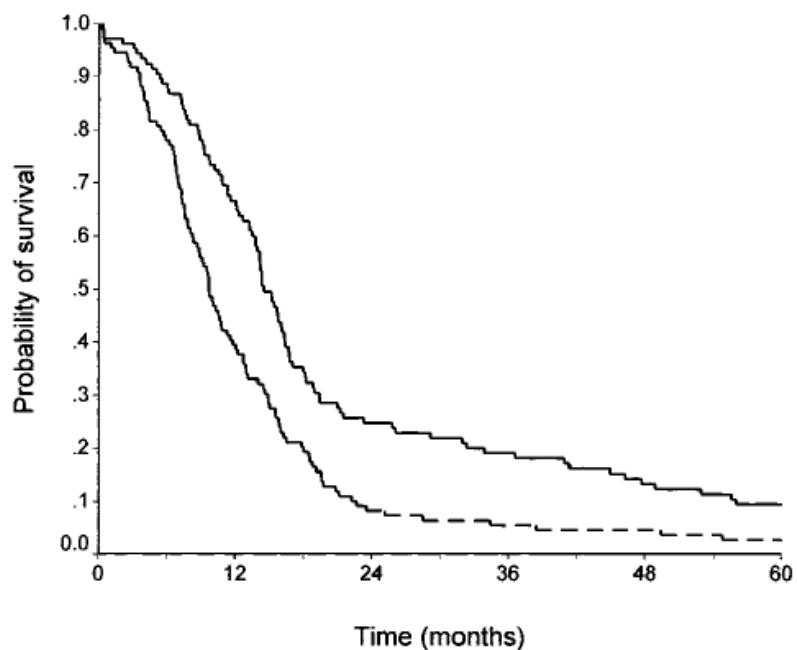


# Småcellet lungekreft

- Ca 15% av alle med lungekreft i Norge
- Ubehandlet ofte aggressiv sykdom med stor tendens til metastasering
- Cytostatika er basisbehandling
- Samtidig thoraxbestrålning øker overlevelsen dersom alle lesjoner kan inkluderes i et tolerabelt strålefelt (limited disease, LD)
- Profylaktisk hjernebestrålning reduserer risikoen for hjernemetastaser og forlenger overlevelsen både ved LD og ED

## Cisplatin and Etoposide Regimen Is Superior to Cyclophosphamide, Epirubicin, and Vincristine Regimen in Small-Cell Lung Cancer: Results From a Randomized Phase III Trial With 5 Years' Follow-Up

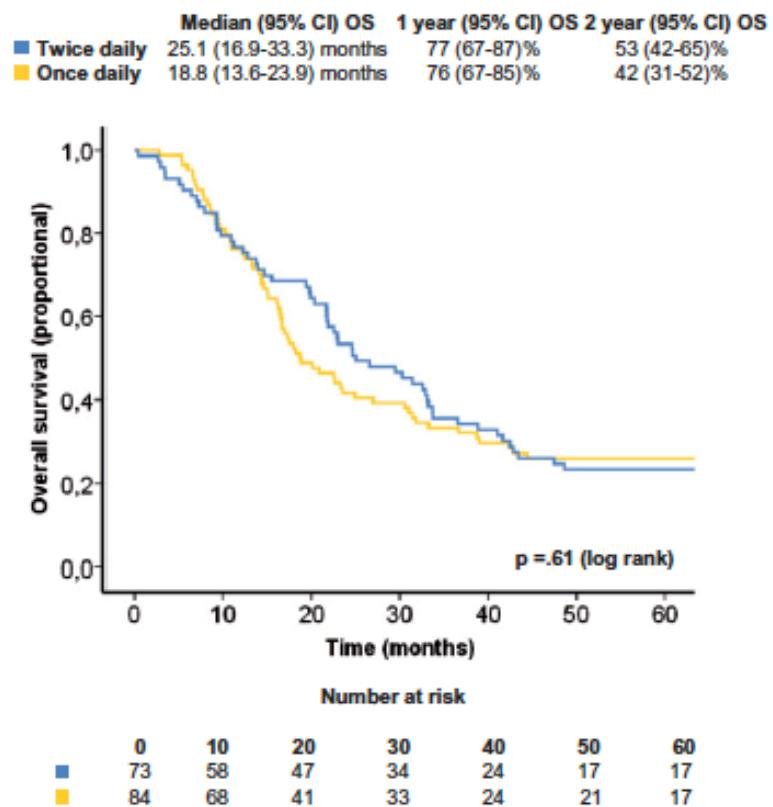
By Stein Sundstrøm, Roy M. Bremnes, Stein Kaasa, Ulf Aasebø, Reidulf Hatlevoll, Ragnar Dahle, Nils Boye, Mari Wang, Tor Vigander, Jan Vilsvik, Eva Skovlund, Einar Hannisdal, and Steinar Aamdal for the Norwegian Lung Cancer Study Group



J Clin Oncol, 2002

Randomized phase II trial comparing twice daily hyperfractionated with once daily hypofractionated thoracic radiotherapy in limited disease small cell lung cancer

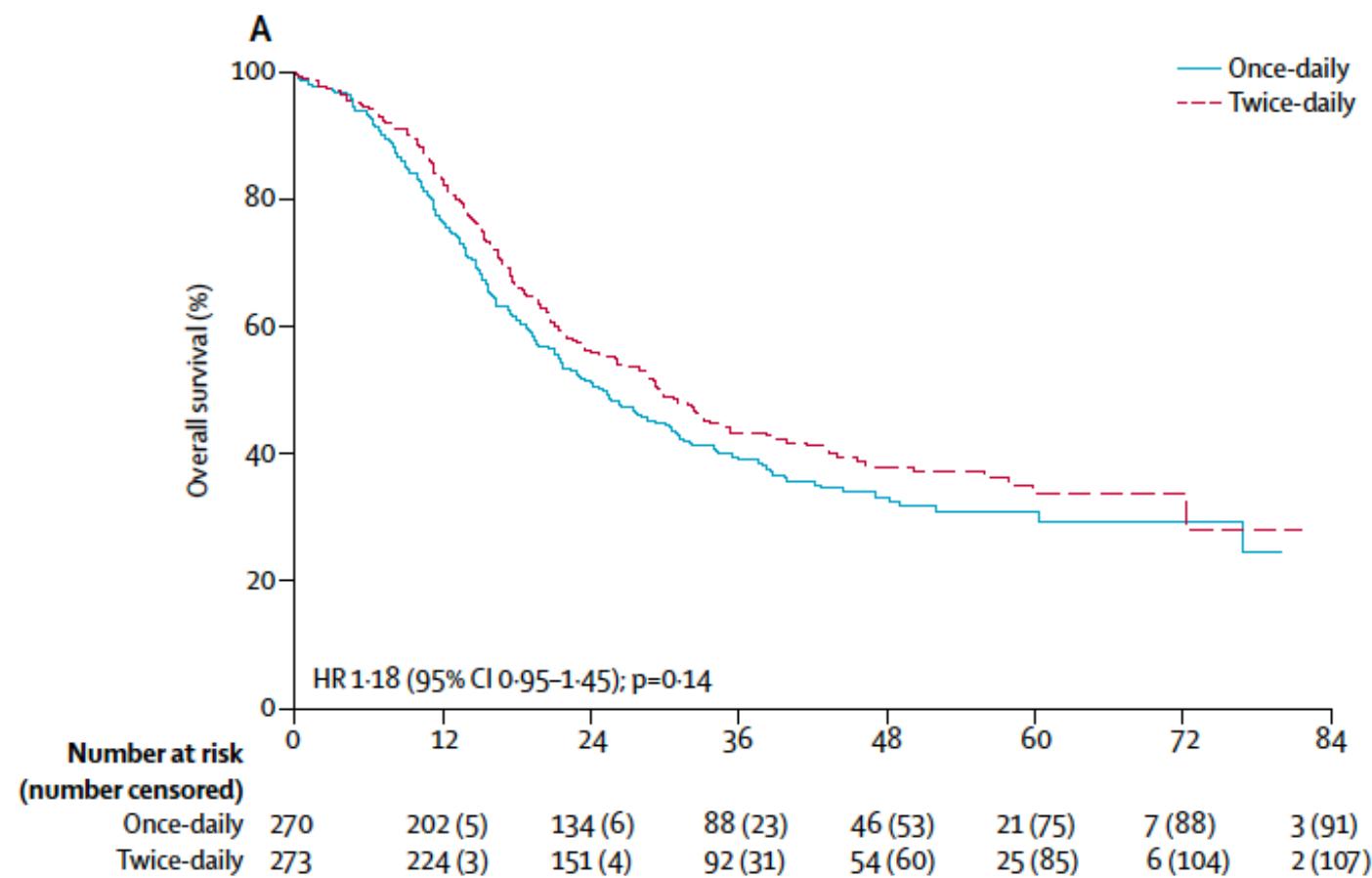
Bjørn H. Grønberg, Tarje O. Halvorsen, Øystein Fløtten, Odd T. Brustugun, Paal F. Brunsvig, Ulf Aasebø, Roy M. Bremnes, Terje Tollåli, Kjersti Hornslien, Bjørg Y. Aksnessæther, Erik D. Liaaen, Stein Sundstrøm & on behalf of the Norwegian Lung Cancer Study Group



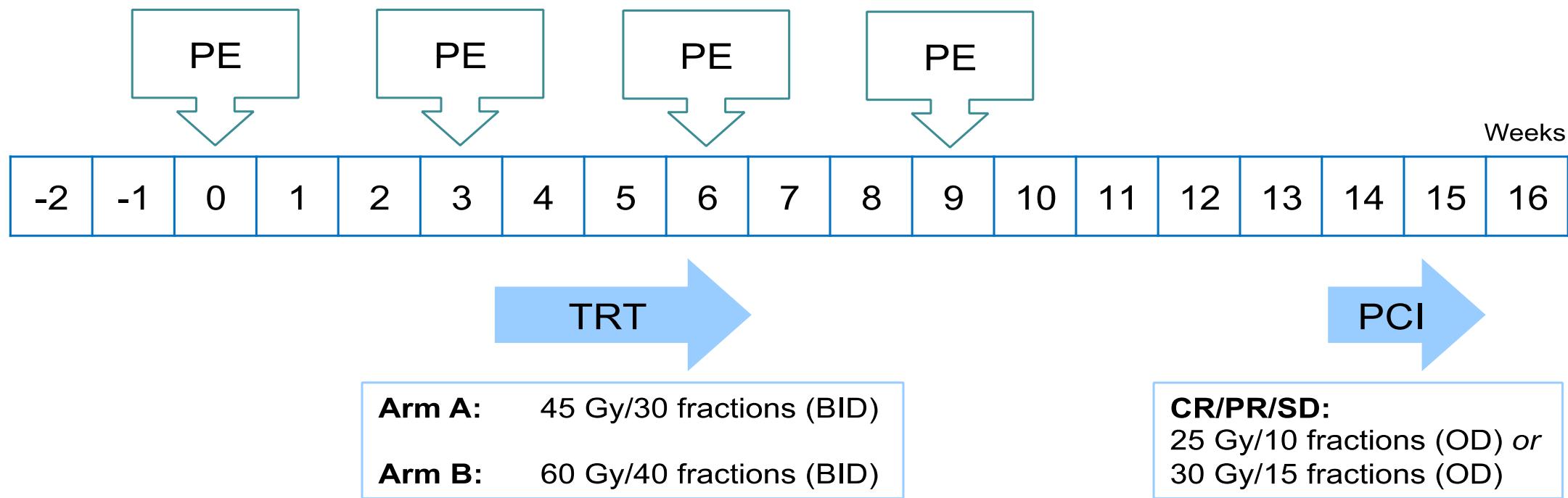
Acta Oncol, 2015

**Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial**

Corinne Faivre-Finn, Michael Snee, Linda Ashcroft, Wiebke Appel, Fabrice Barlesi, Adityanarayan Bhatnagar, Andrea Bezjak, Felipe Cardenal, Pierre Fournel, Susan Harden, Cecile Le Pechoux, Rhona McMenemin, Nazia Mohammed, Mary O'Brien, Jason Pantarotto, Veerle Surmont, Jan P Van Meerbeek, Penella J Woll, Paul Lorigan, Fiona Blackhall, for the CONVERT Study Team

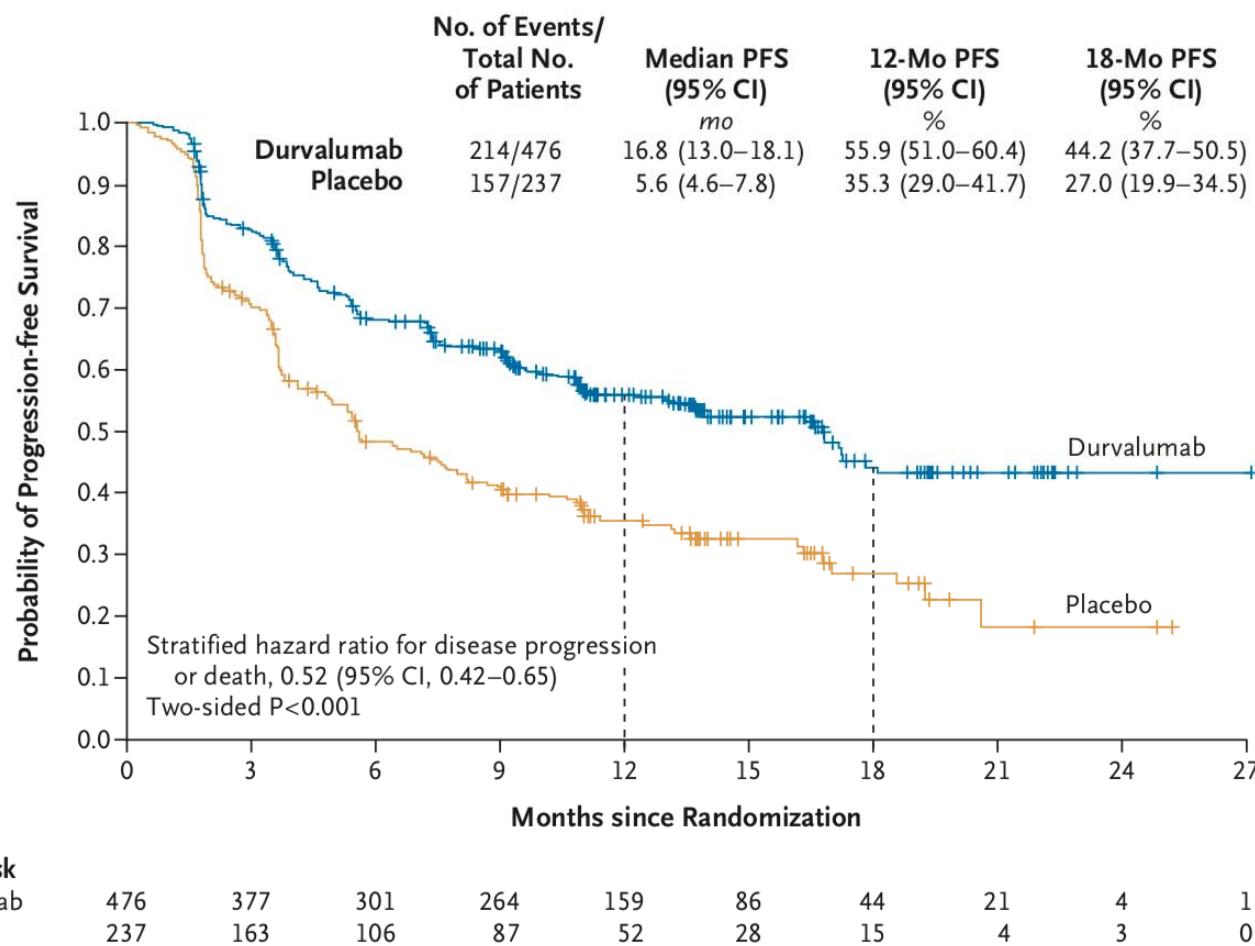


# THORA-studien



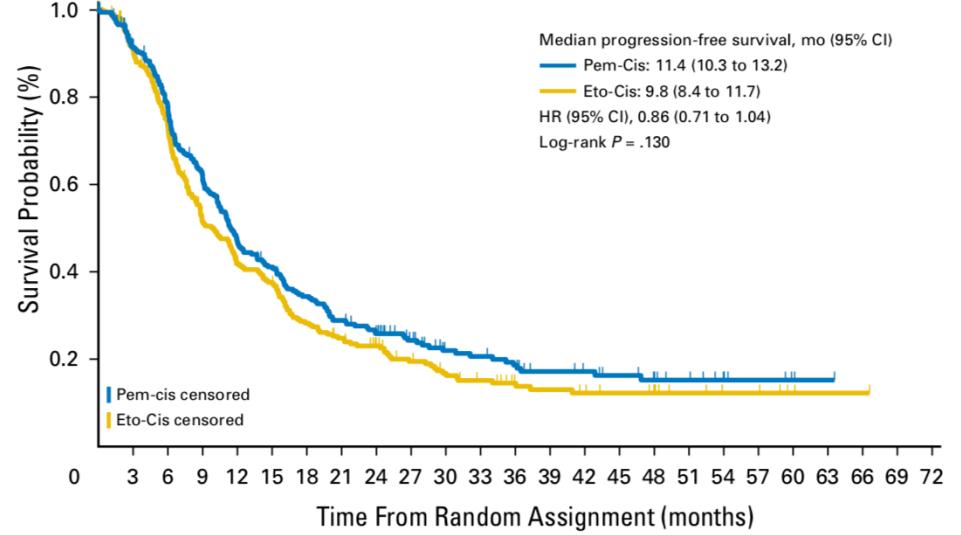
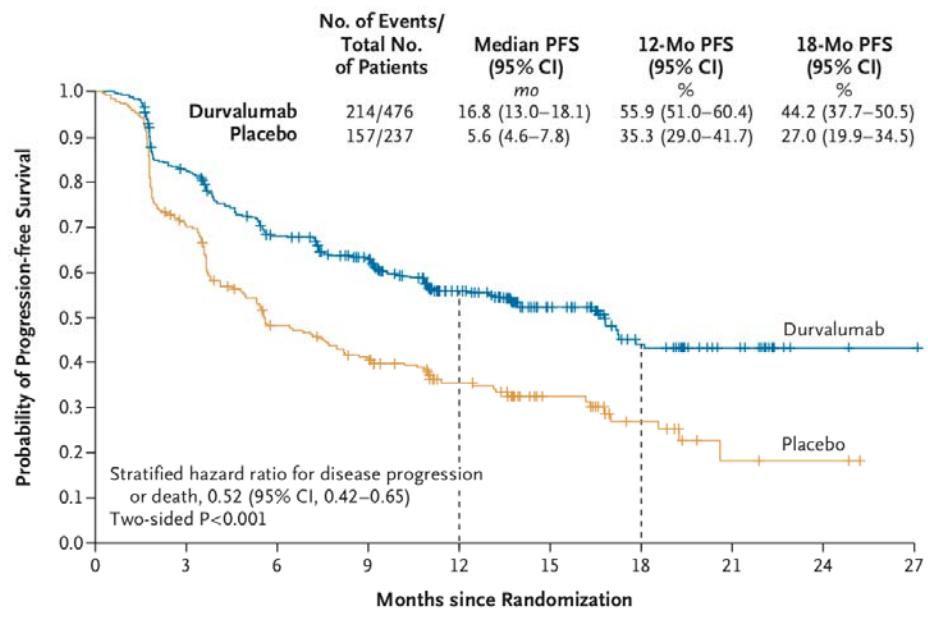
# Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer

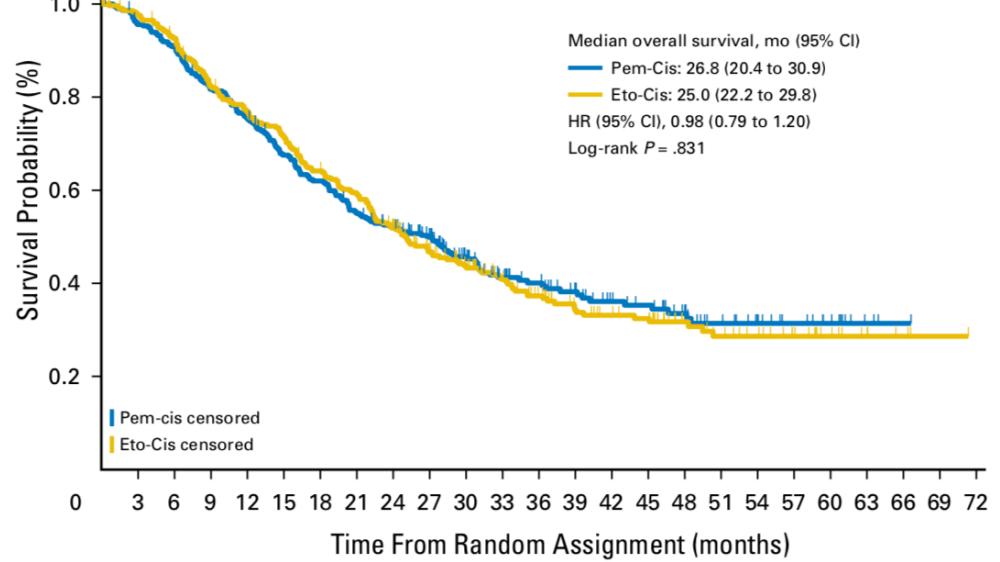
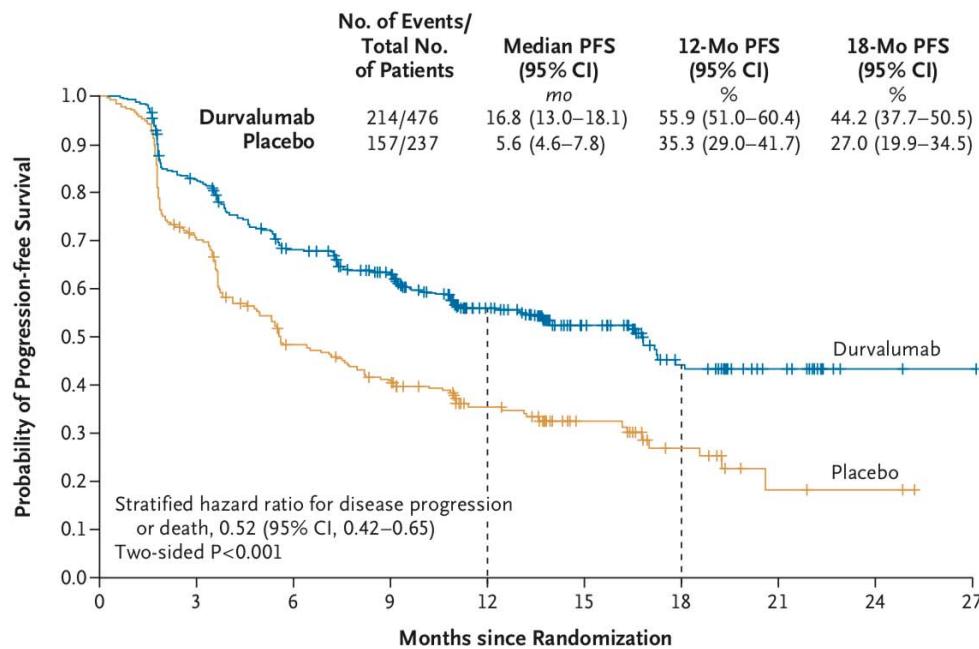
S.J. Antonia, A. Villegas, D. Daniel, D. Vicente, S. Murakami, R. Hui, T. Yokoi, A. Chiappori, K.H. Lee, M. de Wit, B.C. Cho, M. Bourhaba, X. Quantin, T. Tokito, T. Mekhail, D. Planchard, Y.-C. Kim, C.S. Karapetis, S. Hiret, G. Ostoros, K. Kubota, J.E. Gray, L. Paz-Ares, J. de Castro Carpeño, C. Wadsworth, G. Melillo, H. Jiang, Y. Huang, P.A. Dennis, and M. Özgüroğlu, for the PACIFIC Investigators\*



**Table 2.** Antitumor Activity in the Intention-to-Treat Population.\*

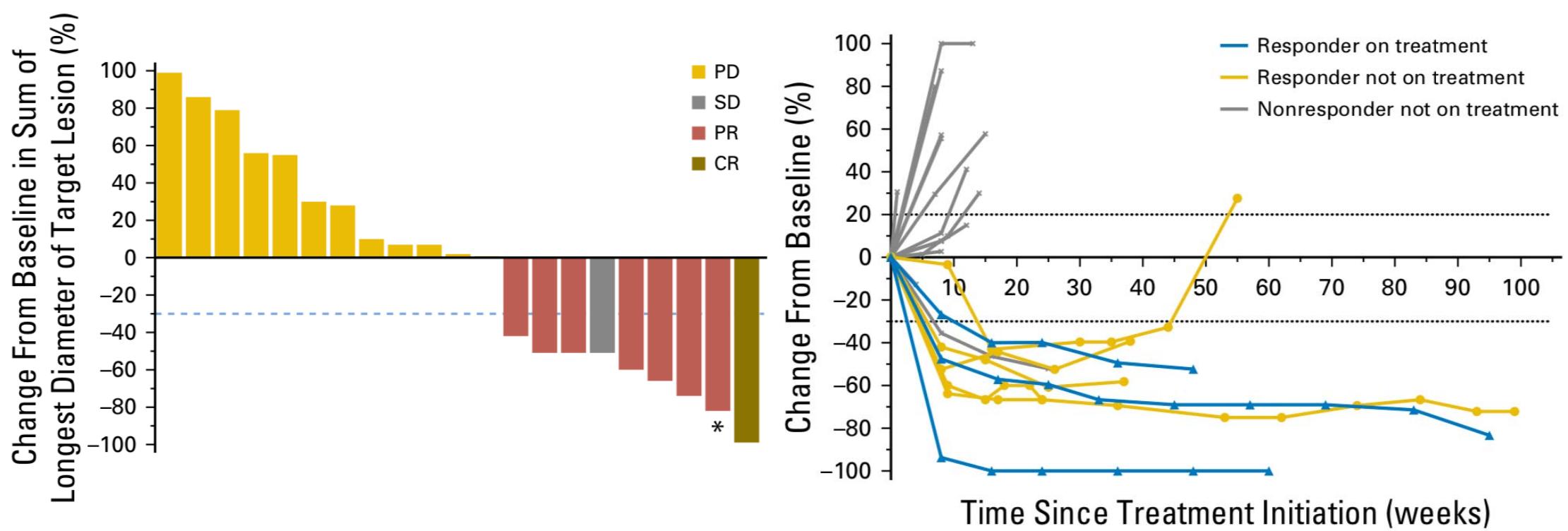
Variable	Durvalumab (N=443)†	Placebo (N=213)†	Treatment Effect‡	P Value
Objective response				
No. of patients with response	126	34		
% of patients (95% CI)	28.4 (24.3–32.9)	16.0 (11.3–21.6)	1.78 (1.27–2.51)	<0.001
Best overall response — no. (%)§				
Complete response	6 (1.4)	1 (0.5)		
Partial response	120 (27.1)	33 (15.5)		
Stable disease	233 (52.6)	119 (55.9)		
Progressive disease	73 (16.5)	59 (27.7)		
Could not be evaluated	10 (2.3)	1 (0.5)		
Duration of response — mo				
Median	NR	13.8	0.43	
95% CI		6.0–NR	0.22–0.84	
Ongoing response at data cutoff point — %¶				
At 12 mo	72.8	56.1		
At 18 mo	72.8	46.8		





# Pembrolizumab in Patients With Extensive-Stage Small-Cell Lung Cancer: Results From the Phase Ib KEYNOTE-028 Study

Patrick A. Ott, Elena Elez, Sandrine Hiret, Dong-Wan Kim, Anne Morosky, Sanatan Saraf, Bilal Piperdi, and Janice M. Mehnert

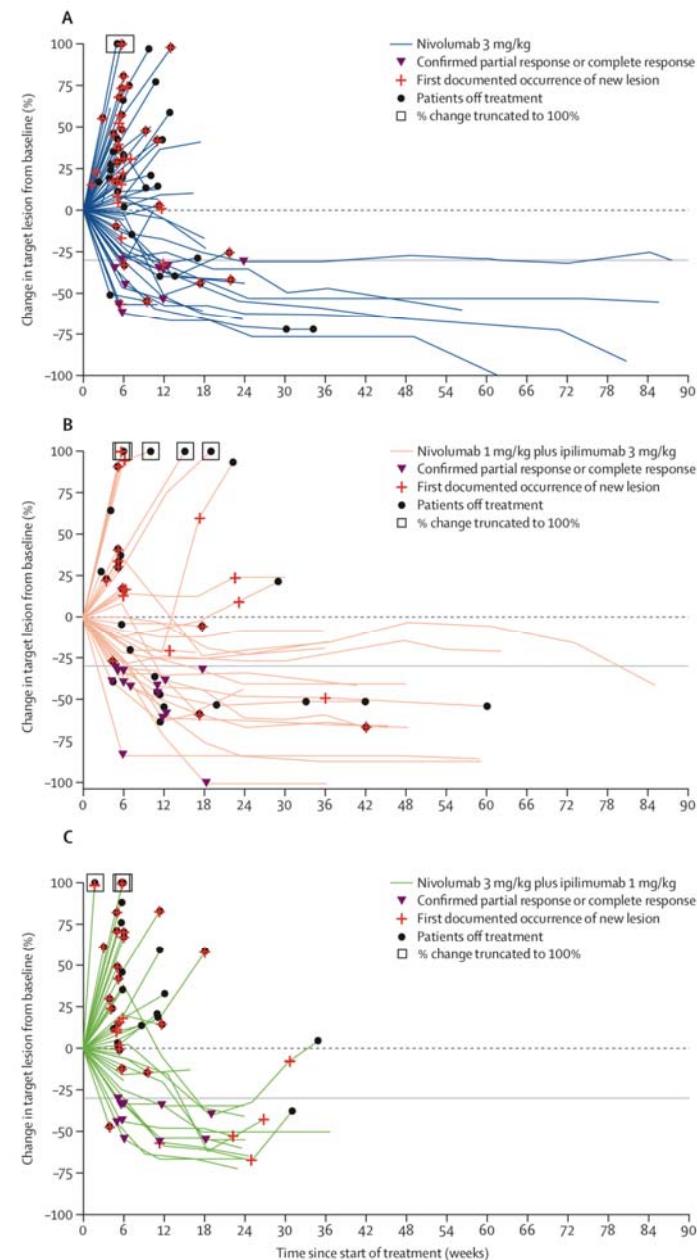


# Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial

Scott J Antonia, José A López-Martin, Johanna Bendell, Patrick A Ott, Matthew Taylor, Joseph Paul Eder, Dirk Jäger, M Catherine Pietanza, Dung T Le, Filippo de Braud, Michael A Morse, Paolo A Ascierto, Leora Horn, Asim Amin, Rathi N Pillai, Jeffry Evans, Ian Chau, Petri Bono, Akin Atmaca, Padmanee Sharma, Christopher T Harbison, Chen-Sheng Lin, Olaf Christensen, Emiliano Calvo

	Nivolumab 3 mg/kg (n=98)	Nivolumab 1 mg/kg plus ipilimumab (n=61)	Nivolumab 3 mg/kg plus ipilimumab (n=54)
Objective response; 95% CI	10 (10%; 5–18)	14 (23%; 13–36)	10 (19%; 9–31)
Best overall response			
Complete response	0	1 (2%)	0
Partial response	10 (10%)	13 (21%)	10 (19%)
Stable disease	22 (22%)	13 (21%)	9 (17%)
Progressive disease	52 (53%)	23 (38%)	29 (54%)
Unable to determine	12 (12%)	8 (13%)	6 (11%)
Not reported	2 (2%)	3 (5%)	0
Time to objective response (IQR), months	2.0 (1.3–2.8)	2.1 (1.4–2.8)	1.4 (1.3–2.7)
Data are n (%) unless otherwise stated. All patients were enrolled at least 90 days prior to database lock.			

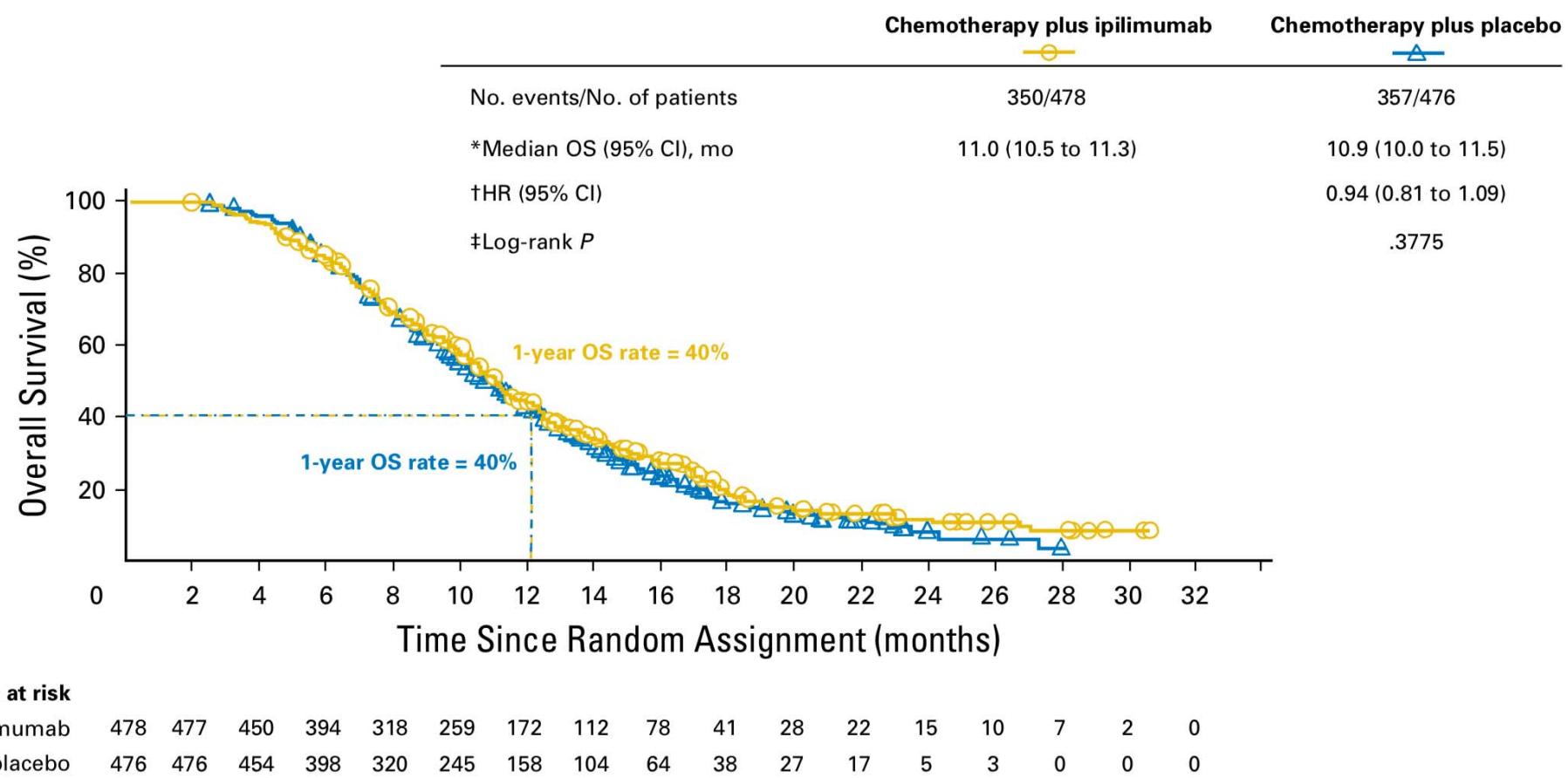
Table 2: Tumour response



# Phase III Randomized Trial of Ipilimumab Plus Etoposide and Platinum Versus Placebo Plus Etoposide and Platinum in Extensive-Stage Small-Cell Lung Cancer

Martin Reck, Alexander Luft, Aleksandra Szczesna, Libor Havel, Sang-We Kim, Wallace Akerley, Maria Catherine Pietanza, Yi-long Wu, Christoph Zielinski, Michael Thomas, Enriqueta Felip, Kathryn Gold, Leora Horn, Joachim Aerts, Kazuhiko Nakagawa, Paul Lorigan, Anne Pieters, Teresa Kong Sanchez, Justin Fairchild, and David Spigel

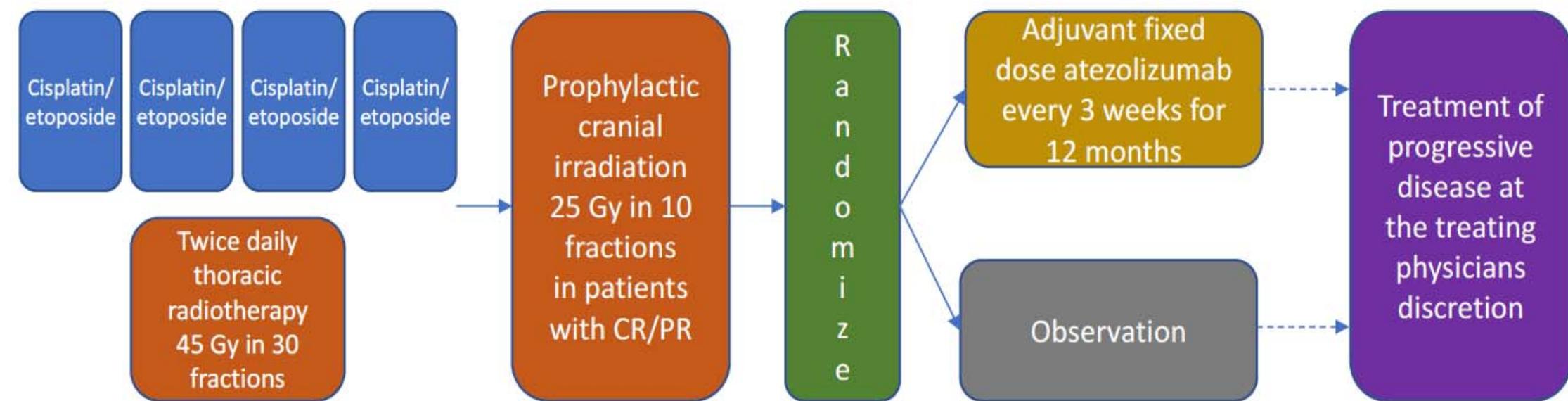
**A**







# ACHILES Design



# Endpoints

**Primary endpoint** Overall survival

**Secondary endpoints** Best response rates  
Progression free survival  
Toxicity  
Health related quality of life

**Exploratory analyses** Prognostic and predictive role of clinical characteristics and biomarkers in tissue, blood and urine. Currently, ctDNA-analyses appears to be the most promising approach for identifying those who are cured after chemoradiotherapy, while PD-L1 and tumor mutational burden are candidate predictive biomarkers for efficacy of atezolizumab.  
Benefit and tolerability of atezolizumab among PS 2 patients compared with the control arm. Benefit and tolerability of atezolizumab among PS 2 patients compared with PS 0-1 patients.

# Eligibility criteria

- Age  $\geq 18$  years
- Written informed consent
- Histologically or cytologically confirmed small-cell lung cancer
- Stage I-III according to TNM v8 ineligible for surgery provided all lesions can be included in a tolerable radiotherapy field ("limited disease")
- ECOG performance status 0-2
- Measureable disease according to the RECIST 1.1
- Adequate organ function defined
- No malignant cells in pericardial or pleural fluid
- Pulmonary function: FEV1  $> 1$  l or  $> 30\%$  of predicted value and DLCO  $> 30\%$  of predicted value

# Eligibility criteria (cont.)

- No serious concomitant systemic disorders
- No lung disease requiring systemic steroids in doses of >10 mg prednisolone (or equivalent dose of other steroid)
- No previous allogeneic or organ transplant
- No active or history of autoimmune disease or immune deficiency
- No history of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- No live vaccine administered last 30 days, active infection requiring IV antibiotics, no active viral hepatitis or HIV
- No clinically active cancer other than SCLC (breast and prostate cancer on hormonal therapy is allowed)
- No pregnancy or lactating women

# Eligibility for randomization

- Completed four courses of platinum plus etoposide and thoracic radiotherapy of 45 Gy
- Non-progression at CT evaluation 2-3 weeks after the last chemotherapy-course
- ECOG performance status 0-2
- Negative pregnancy test in women of childbearing potential

# Sample size

- To detect an improvement in 2-year survival from 53% to 66%, 80 patients are required on each arm
- We expect a drop-out rate of max. 25% and aim to include a total of 212 patients

# Deltakende sykehus

- 6 svenske sykehus
- 7 danske sykehus
- Vilnius
- Alle store sykehus i Norge – alle får være med!

# Status

- Protokoll godkjent
- Første pasient inkluderes i mai!?