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ESTRO 36 update

F. Würschmidt

Radiologische Allianz, Hamburg

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 Meerbeeck, Penella J Woll, Paul Lorigan, Fiona Blackhall, for the CONVERT Study Team

Lancet Oncol 2017 published online 19 June 2017

SCLC

- **Konventionelle einmal tägliche RT oder hyperfraktioniert-akzeleriert (2 x tgl. 1.5 Gy)?**
  - CONVERT trial
    - n=547
    - 45 Gy/1.5 Gy bid vs 66 Gy/2 Gy starting on day 22 after Cisplatin/Etoposid

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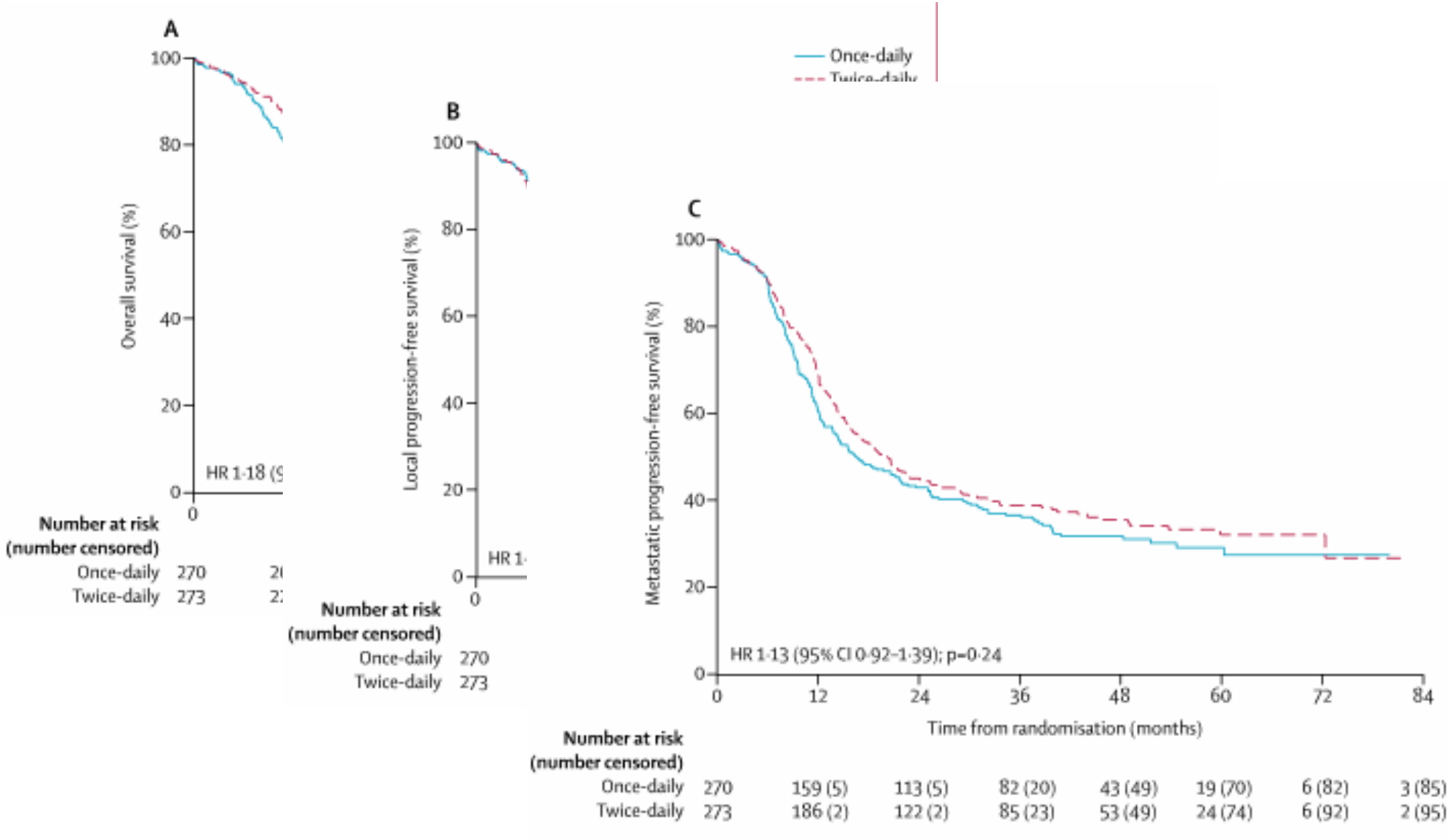
CONVERT trial



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CONVERT trial

Adverse events in the population assessed for radiotherapy toxicity (n=254 in the twice-daily group; n=246 in the once-daily group)									
Oesophagitis	159 (63%)	46 (18%)	1 (<1%)	..	135 (54%)	47 (19%)	..	..	0·85
Pneumonitis	51 (20%)	3 (1%)	1 (<1%)	1 (<1%)	49 (19%)	3 (1%)	1 (<1%)	2 (1%)	0·70

	Twice-daily group (n=248)			Once-daily group (n=233)			p value*
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4	
Dermatitis	15 (6%)	..	..	17 (7%)	..	..	..
Oesophagitis	29 (12%)	..	..	39 (17%)	4 (2%)	..	0·06
Oesophageal stricture or fistula	8 (3%)	..	..	6 (3%)	1 (<1%)	..	0·48
Pulmonary fibrosis	119 (48%)	3 (1%)	..	106 (46%)	2 (1%)	..	>0·99
Pneumonitis	71 (29%)	5 (2%)	1 (<1%)	70 (30%)	5 (2%)	1 (<1%)	0·90
Myelitis	1 (<1%)†	..	..	8 (3%)†	..	..	..
Other	131 (53%)	20 (8%)	3 (1%)	113 (49%)	18 (8%)	2 (1%)	0·78

Data are n (%). *p values calculated for grade 3–4 adverse events. †All cases of myelitis were grade 1 adverse events.

Table 5: **Late adverse events (>3 months after study treatment)**

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CONVERT trial in limited disease SCLC

- **Konventionelle einmal tägliche RT oder hyperfraktioniert-akzeleriert** CONVERT trial
  - n=547
  - 45 Gy/1.5 Gy bid vs 66 Gy/2 Gy starting on day 22 after Cisplatin/Etoposid

- **Kein Unterschied im Überleben**
  - OS: 31% (66 Gy) vs 34% (45 Gy bid)
    - Intergroup 0096: 16-26%
- **Akute und späte Therapiefolgen gleich** und niedriger als erwartet:
  - Ösophagitis Grad 4: 19%
  - Pneumonitis Grad 3-4: 2%
- PET-CT staging, 3D-RT / IMRT, keine elektive Lymphknoten-RT
- **Comment Prof. Fietkau, Univ. Erlangen: "However, for patients for whom this regimen is not feasible for logistical reasons, or in whom there is an increased risk or grade 4 neutropenia, a regimen using once-daily radiotherapy in combination with an increased total dose could be seen as an acceptable alternative". *Lancet Oncol 2017 online first 19 June 2017***

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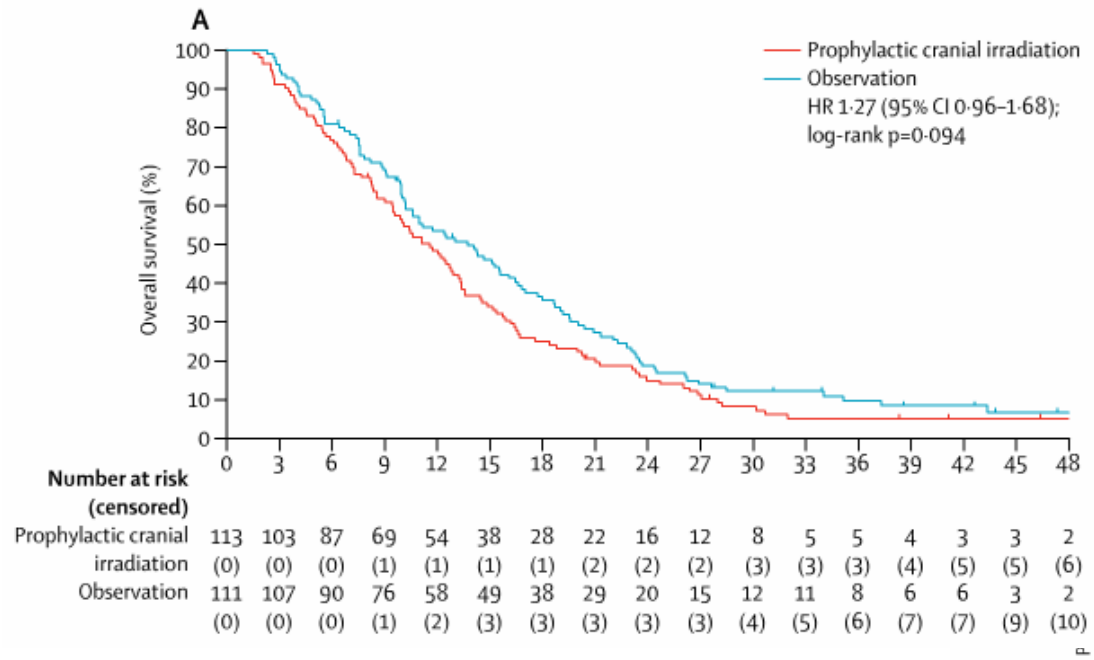
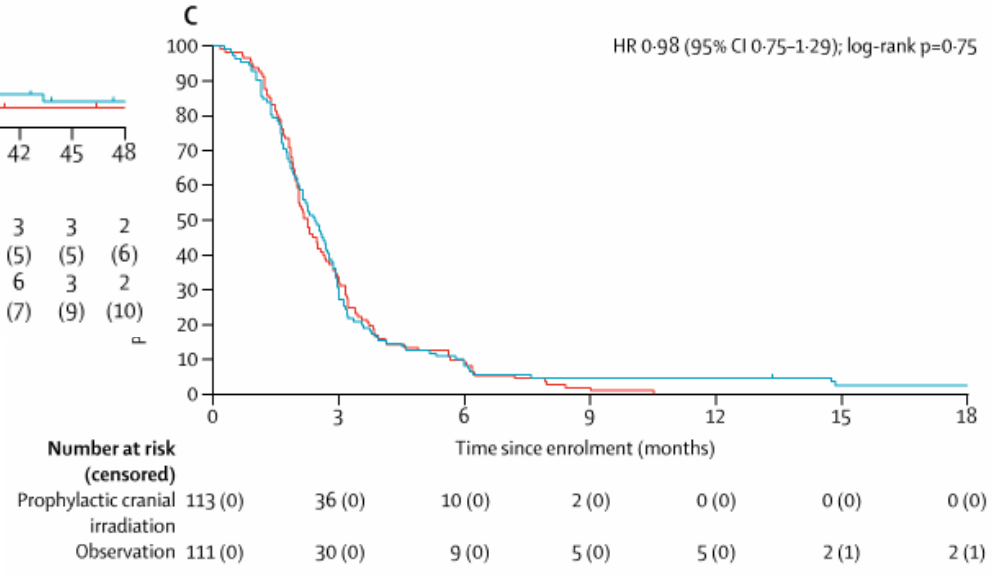
SCLC- prophylaktische Ganzhirn-RT

- **Prophylaktische Ganzhirn-RT** bei limited disease
  - Wenn Staging **inkl. cMRT** kein Hinweis auf zerebrale Metastasen ergibt





Takahashi et al.; The Lancet Oncology. 2017

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ESPATUE Studie
Stuschke et al. ESTRO 36, 2017

- NSCLC im Stadium IIIA
- Induktionschemotherapie gefolgt von Chemoradiotherapie
  - Randomisierung: Operation vs weitere Chemoradiotherapie
- Lokalrezidivraten < 20%
- Wichtigster Prognosefaktor: pCR
- Problem: Hirnmetastasen

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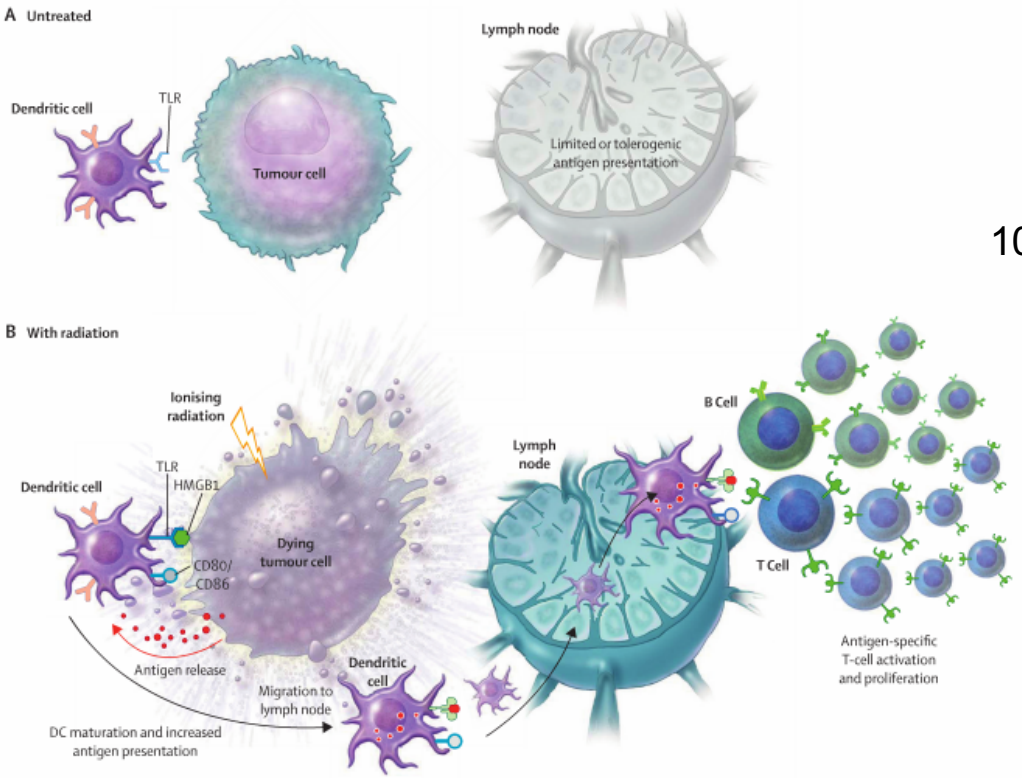
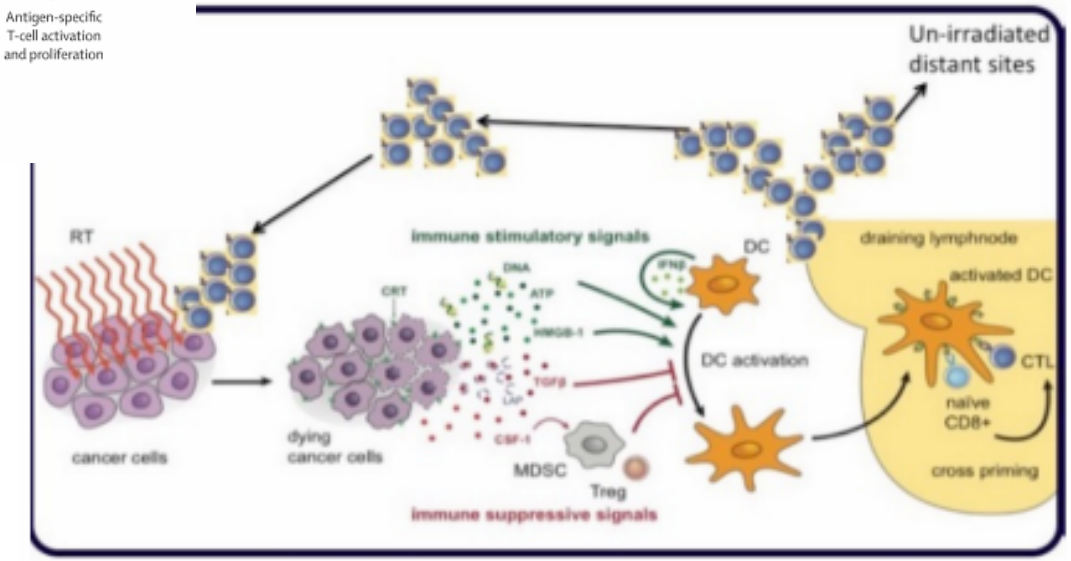
Abscopal effects
Immunmodulation durch Radiotherapie



Sharabi et al. The Lancet Oncology. 2015, DOI: 10.1016/S1470-2045(15)00007-8,



Formenti et al. ESTRO 2017

Abscopal responses in metastatic non-small cell lung cancer (NSCLC): a phase II study combined radiotherapy and ipilimumab
Formenti et al.; Cornell Univ. New York, USA
ESTRO 36: Radiother Oncol Vol 123 S.1 May 2017; SP -0012

- Chemotherapie-refraktäre NSCLC mit 2 meßbaren Läsionen
  - 41% mit Hirnmetastasen
- ECOG 0 – 2
- 5 x 6 Gy auf 1 Läsion (z.B. symptomatische)
- Ipilimumab (3mg/kg iv) alle 3 Wochen x 3; innerhalb 24 Stunden nach RT-Beginn
- N = 39

Abscopal responses in metastatic non-small cell lung cancer (NSCLC): a phase II study combined radiotherapy and ipilimumab
Formenti et al.; Cornell Univ. New York, USA
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- **Abscopal effect** in 18% (intention to treat)
  - 7 Pat. mit 4 Zyklen Ipi: 33%
- mit höherer Überlebenswahrscheinlichkeit
- PD-L1 Expression >10% (vor Therapie) bei CR/PR
- T-Zell Klonalität deutlich verändert
- *Neue Studie*: Ipi + SBRT gefolgt von Ipi + Nivo als Erhaltungstherapie

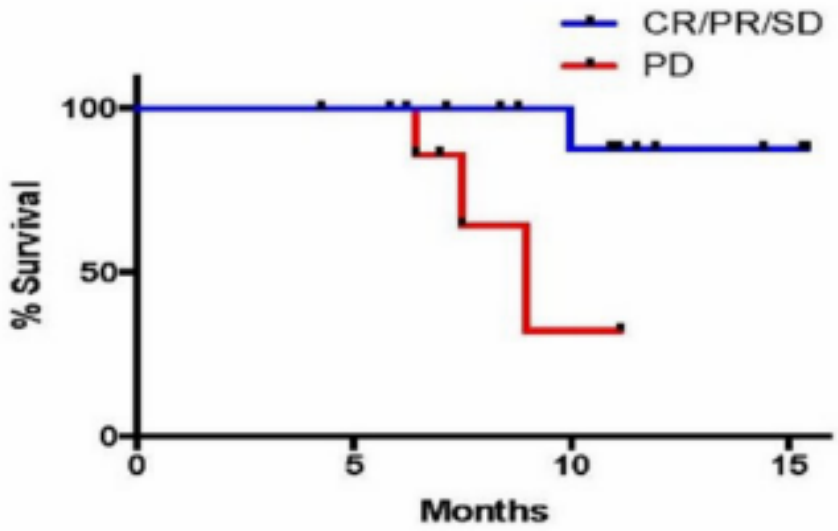

Figure.
Percentage of surviving patients based on abscopal response after ipilimumab and radiotherapy, in a trial of 39 chemo-refractory metastatic NSCLC patients