
LOEWS
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LUNGENCLINIC GROSSHANSDORF

Neues zur Thoraxonkologie: Was sich ändert

D.F. Heigener

Conflicts of Interest:

Honoraria for Presentations, **A**dvisory Boards and **T**ravel Reimbursement

- BMS (H,A,T)
- Roche (H,A,T)
- MSD (H,A,T)
- Boehringer Ingelheim (H,A,T)
- Pfizer (H,A,T)
- Lilly (H,A,T)
- Astra Zeneca (H,A,T)
- Chugai (H,A,T)
- Bayer (H,T)
- Fresenius (A)

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Agenda

- Prophylaktische Kopfbestrahlung beim NSCLC
- Neuer Treiber: MET
- Exkurs: TMB und PD-L1
- Alectinib bei ALK-positiven

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Prophylactic cranial irradiation (PCI) versus observation in radically treated stage III non-small cell lung cancer (NSCLC): a randomized phase III study (NVALT-11)

Groen HJM (1), Dingemans A-M (2), Praag J (3), Belderbos J (4), C. Tissing-Tan C (5), Herder G (6), Haitjema T (7); Ubbels F (1); Lagerwaard J (8); El Sharouni S (9); Stigt J (10); Smit EF (11); van Tinteren H (11), van der Noort V (11), De Ruysscher DKM (2)

1, University Medical Center Groningen; 2, University Medical Center Maastricht, Maastro, Maastricht; 3, Erasmus Medical Center, Rotterdam; 4, Anthonie van Leeuwenhoek hospital, Amsterdam; 5, Radiotherapeutic Institute Arnhem; 6, Meander hospital, Amersfoort; 7, NWZ hospital; 8, Free University Medical Center, Amsterdam; 9, University Medical Center Utrecht; 10, Isala hospital, Zwolle; 11, National Cancer Institute, Amsterdam.

Trial registrered as NTR1601

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Groen et al.; Abstr 8502; ASCO 2017

Endpoints

- Primary endpoint: Proportion of patients developing symptomatic brain metastases.

- Secondary endpoints:

1. Time to develop neurological symptoms (confirmed or unconfirmed by imaging).
2. Side effects by PS and CTCAE 3.0
3. Changes in quality of life (QLQ-C30 and EuroQol 5D).
4. Overall survival.

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Groen et al.; Abstr 8502; ASCO 2017

	PCI (n=86) No of pts (%)	Observation (n=88) No of pts (%)	p
BM by MRI or CT	7 (8.1)	26 (29.7)	0.0004
BM + neuro symptoms*	4 (4.6)	25 (28.4)	< 0.001
Neuro symptoms** without BM	31 (36)	10 (11.3)	0.0001

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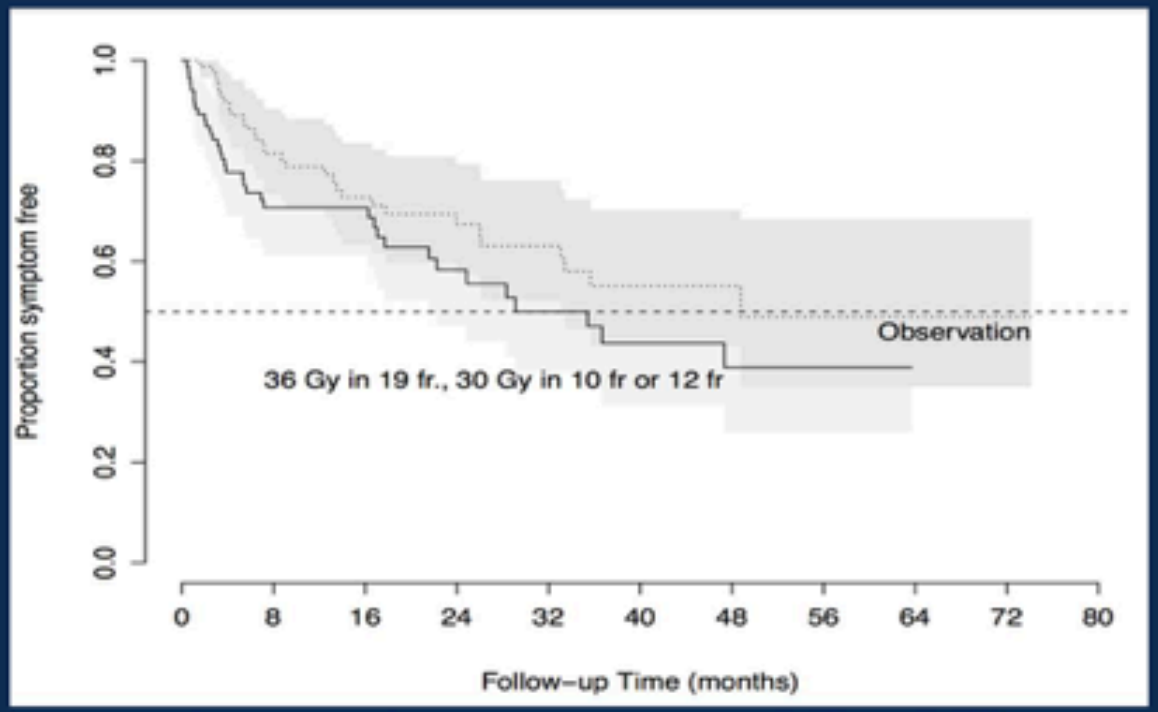
Groen et al.; Abstr 8502; ASCO 2017

Time to all neurological symptoms in stage III NSCLC



Time to develop neurological symptoms was not significantly different (HR 1.1; 95% CI, 0.61 – 1.8, p = 0.73) in spite of the difference in medians: 39.4 (95% CI, 32.9 – 49.5) in the PCI arm and 56.6 mo (95% CI, > 33.3) in the observation arm.

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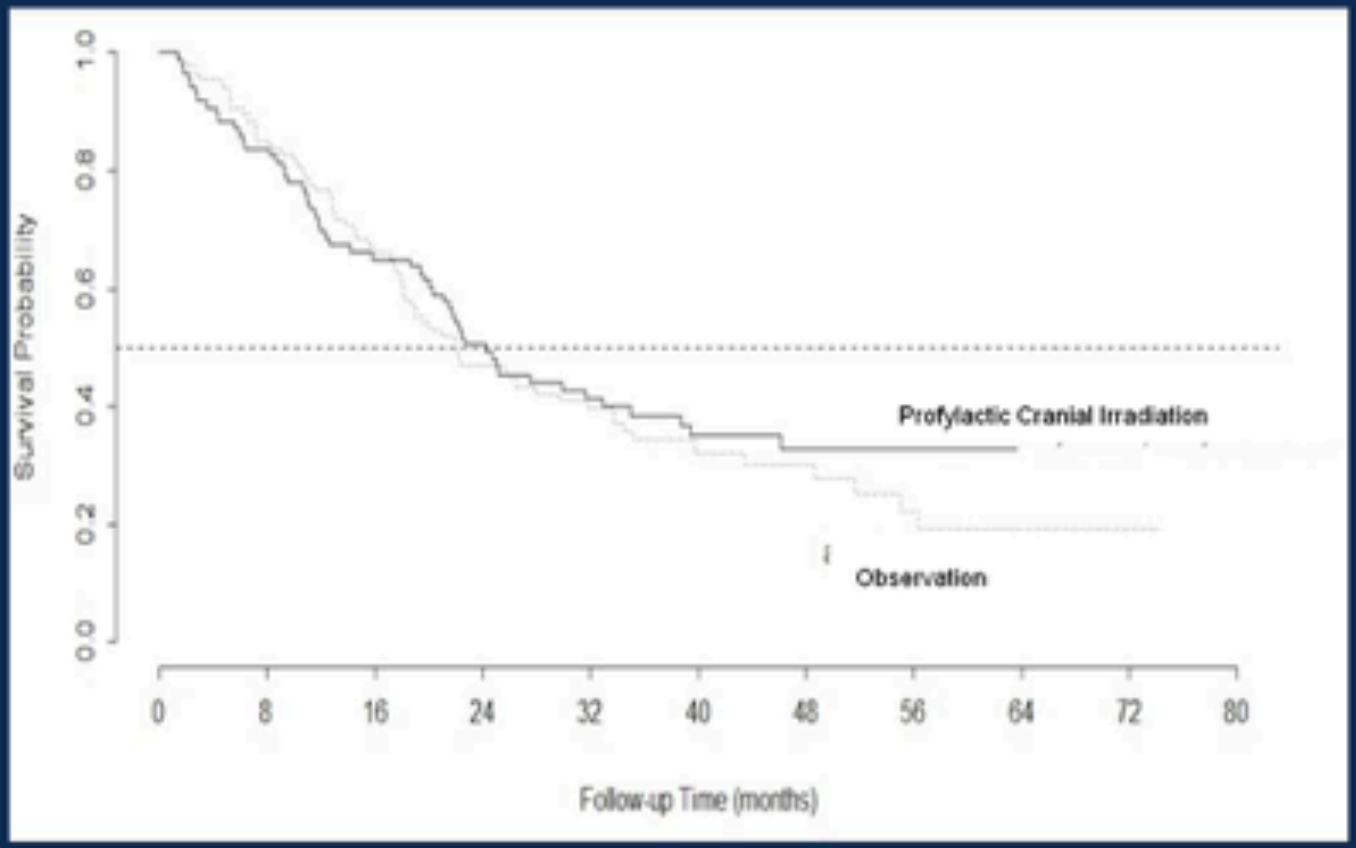
Groen et al.; Abstr 8502; ASCO 2017

Overall survival



Median OS was also not different with 24.2 (95% CI, 20.3-38.7) in PCI and 21.9 mo (95% CI, 18.1 – 33.7) in observation arm (p = 0.52).

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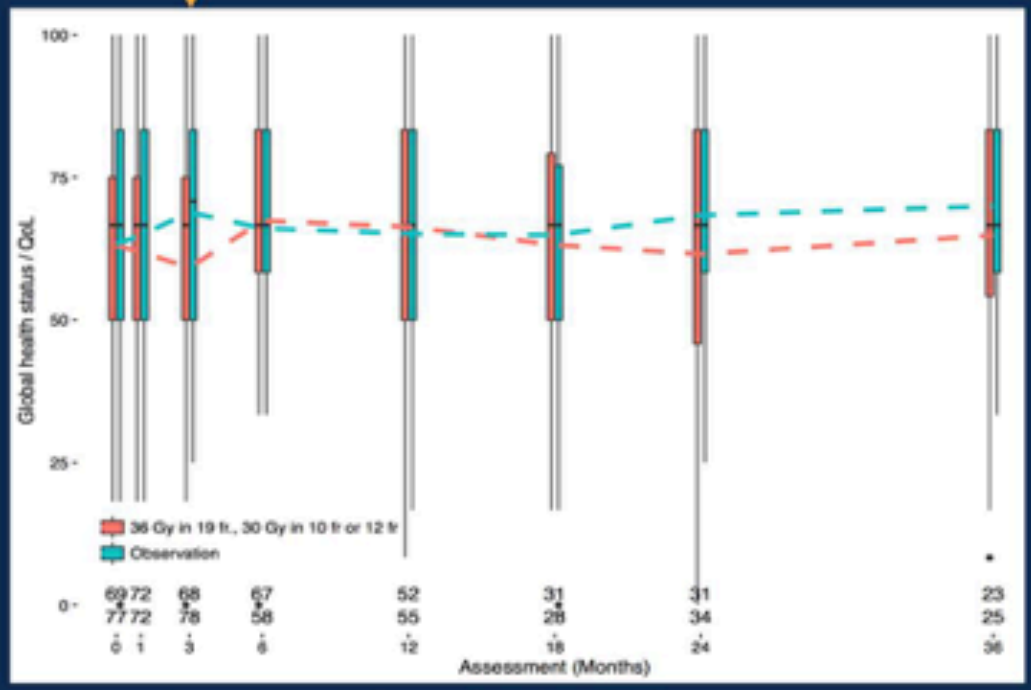
Groen et al.; Abstr 8502; ASCO 2017

Global quality of life by EORTC QCQ



Global quality of life at 3 months after PCI is worse than in observation arm (p=0.02)

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Groen et al.; Abstr 8502; ASCO 2017

Take Home PCI bei NSCLC

- Prophylaktische Neurokraniumbestrahlung senkt die Inzidenz von Hirnmetastasen
- Das nützt dem Patienten aber nichts

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Impact of MET inhibitors on survival among patients with *MET* exon 14 mutant non-small cell lung cancer

Mark M. Awad,[1] Giulia C. Leonardi,[1] Sasha Kravets,[1] Suzanne E. Dahlberg,[1] Alexander Drilon,[2] Sinead A. Noonan,[3] D. Ross Camidge,[3] Sai-Hong Ignatius Ou,[4] Daniel B. Costa,[5] Shirish M. Gadgeel,[6] Conor E. Steuer,[7] Patrick M. Forde,[8] Viola W. Zhu,[9] Yoko Fukuda,[10] Jeffrey W. Clark,[11] Pasi A. Jänne,[1] Tony Mok,[12] Lynette M. Sholl,[13] Rebecca S. Heist[11]

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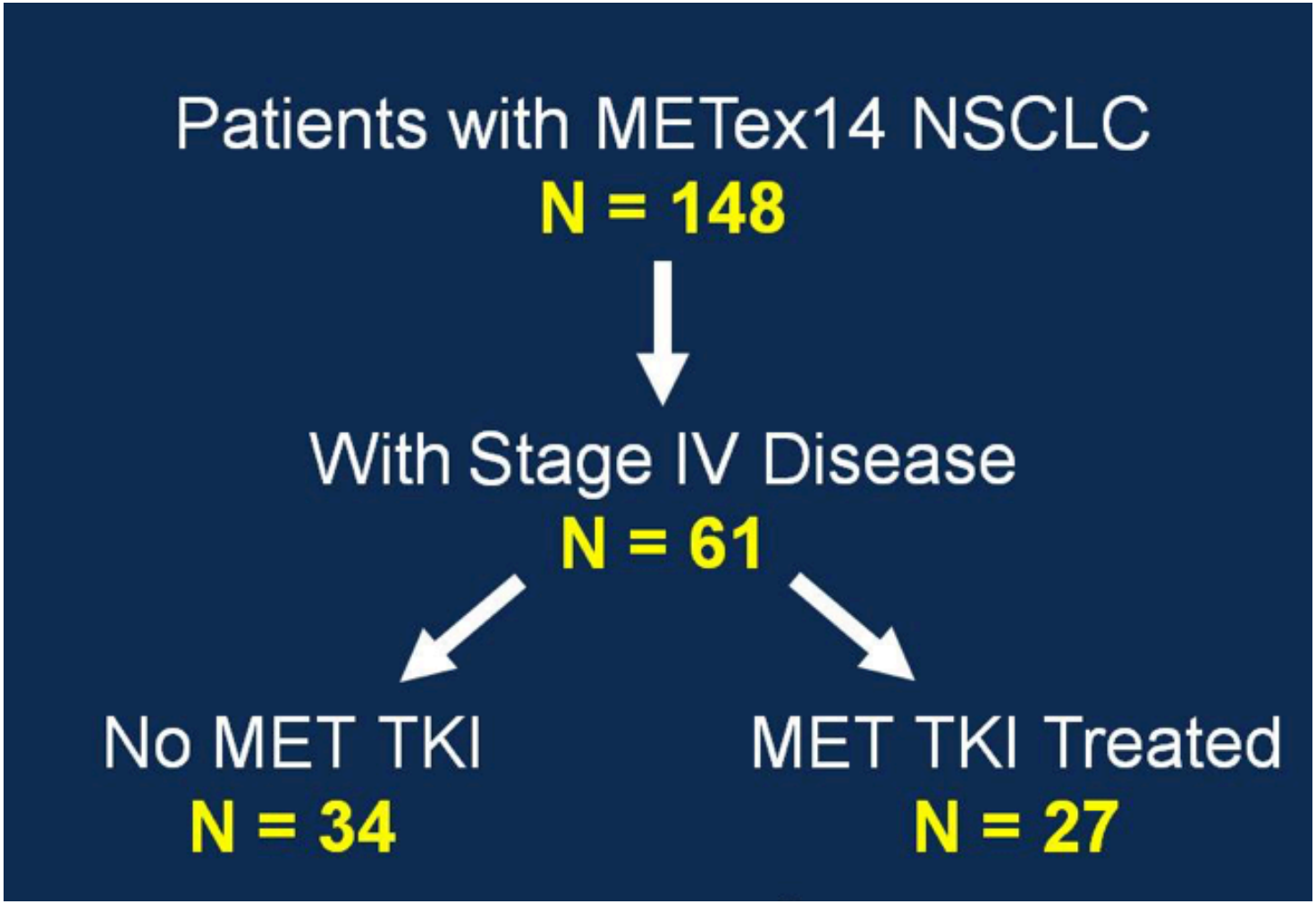
Awad et al; Abstr. 8511; ASCO 2017



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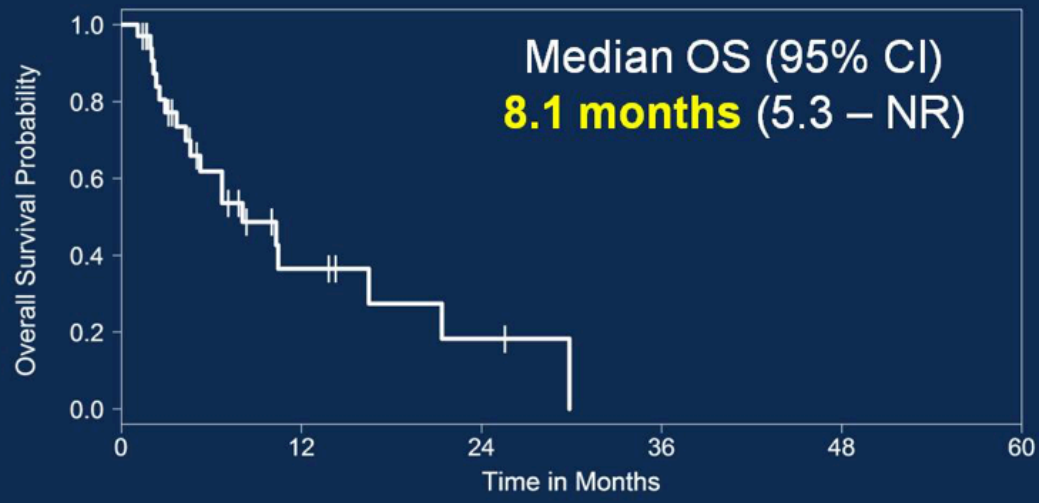
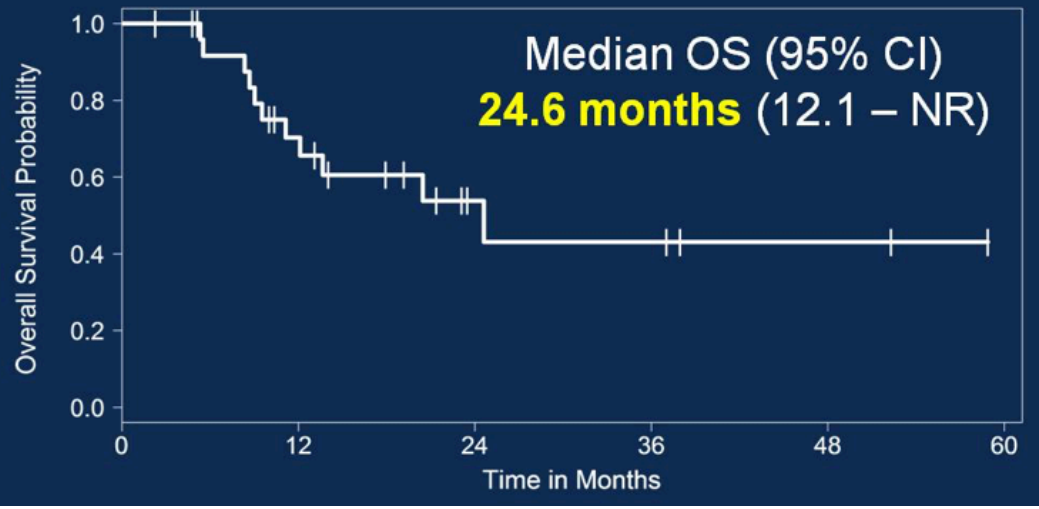
Awad et al; Abstr. 8511; ASCO 2017

Overall survival from date of stage IV diagnosis

Never received
a MET TKI
N = 34



Received
a MET TKI
N = 27



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Awad et al; Abstr. 8511; ASCO 2017

PD-L1 Expression and Response to Immunotherapy in Patients with *MET* Exon 14 Altered Non-Small Cell Lung Cancer

Joshua K. Sabari,[1] Joseph Montecalvo,[1] Ruqin Chen,[1] Jordan Dienstag,[1] Chebli Mrad,[1] Isabella Bergagnini,[1] W. Victoria Lai,[1] Kathryn C. Arbour,[1] Catherine A. Shu,[2] Matthew Hellmann,[1] Paul K. Paik,[1] Gregory J. Riely,[1] Mark G. Kris,[1] Charles M. Rudin,[1] Natasha Rekhtman,[1] Alexander Drilon[1]

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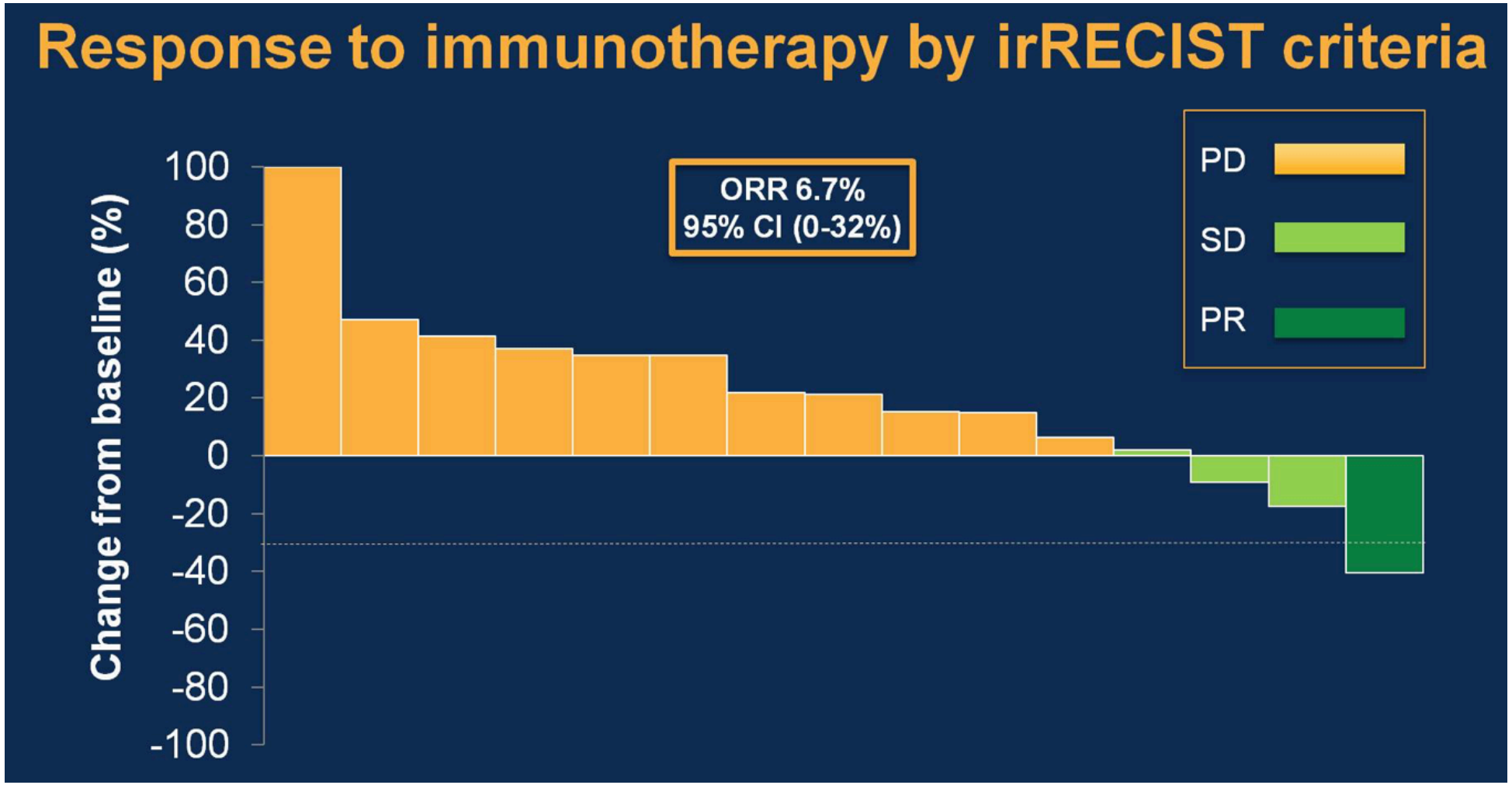
Sabari et al.; Abstr. 8512; ASCO 2017

Response to immunotherapy by irRECIST criteria



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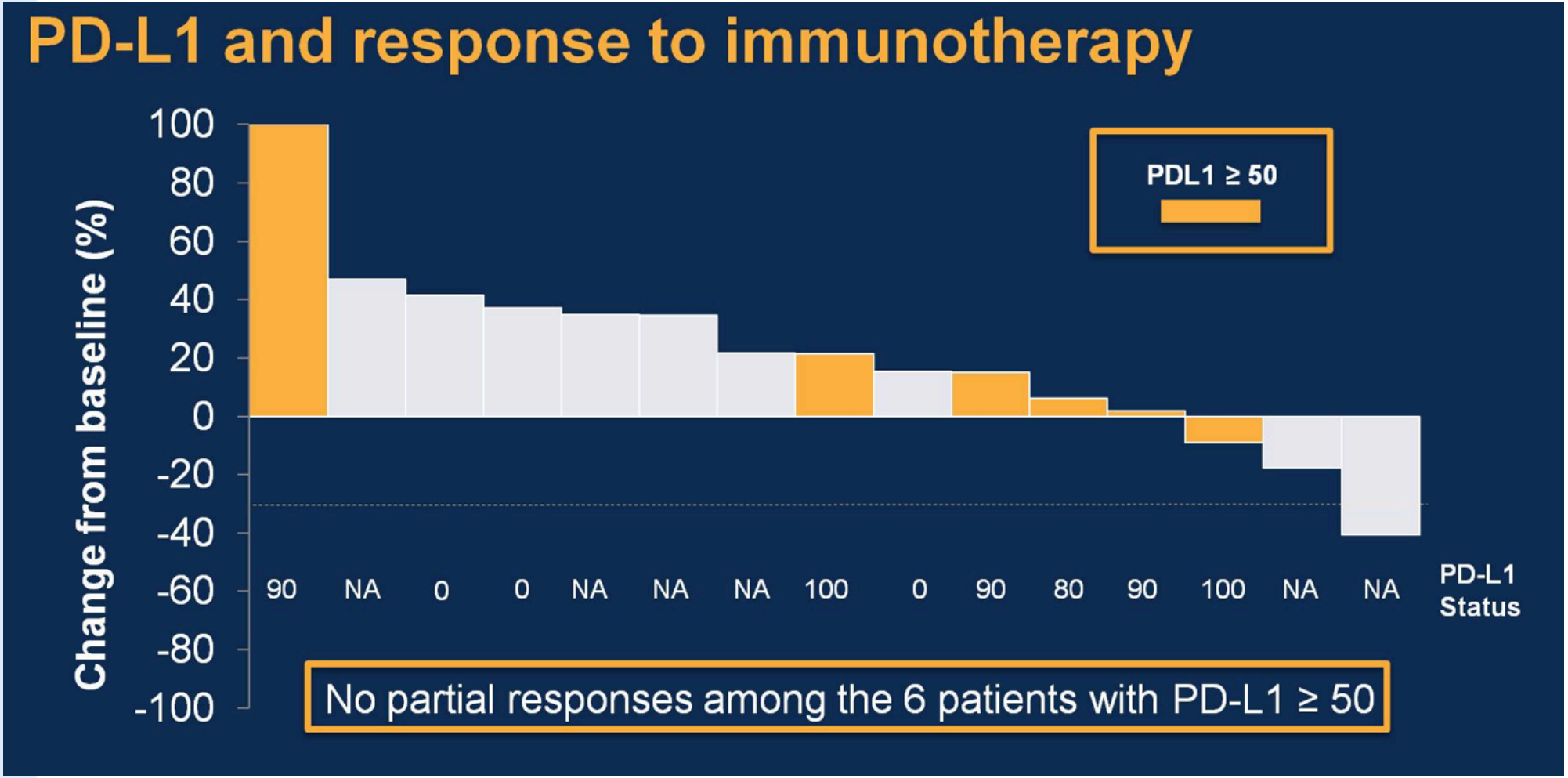
Sabari et al.; Abstr. 8512; ASCO 2017

PD-L1 and response to immunotherapy



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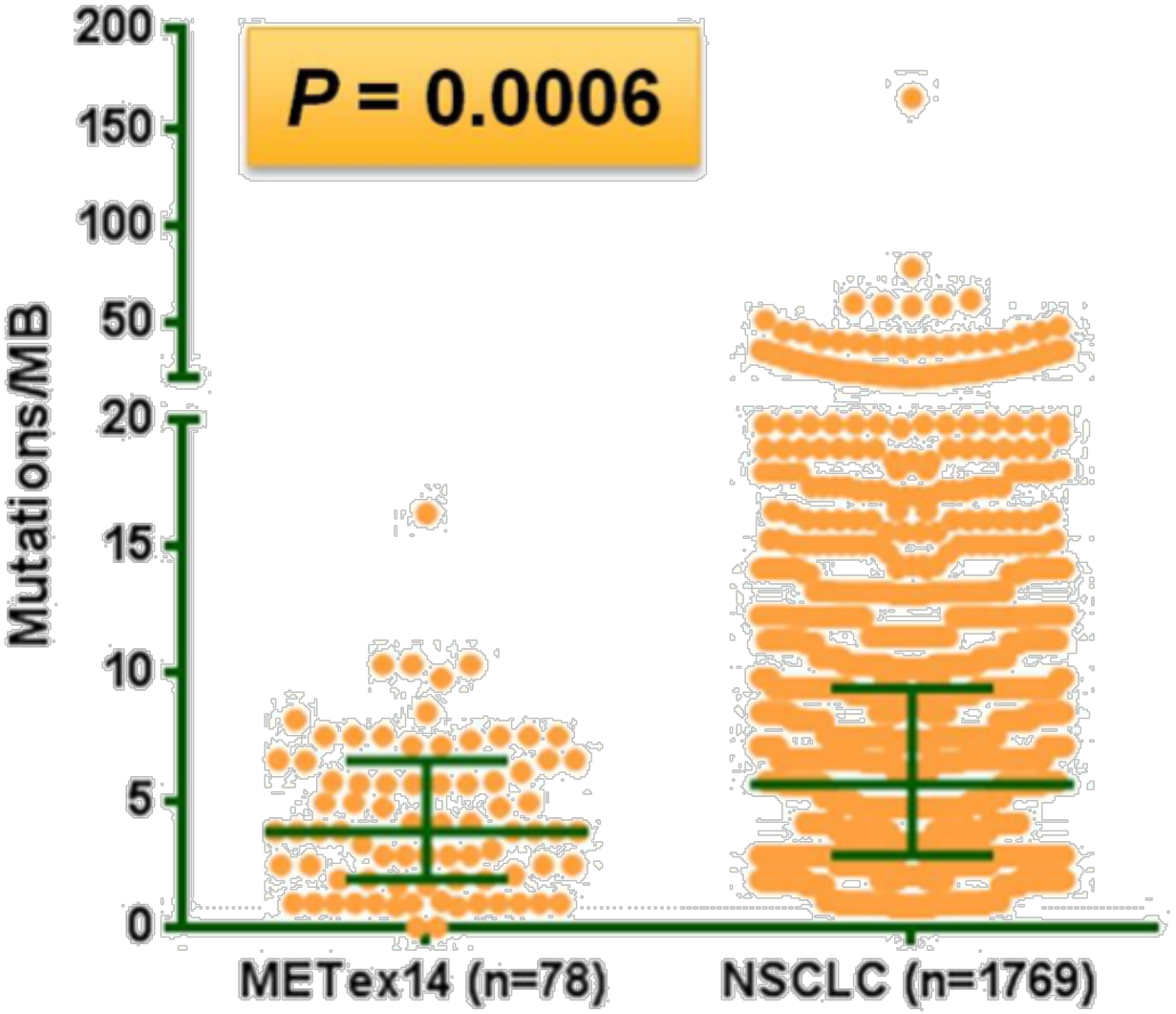
Sabari et al.; Abstr. 8512; ASCO 2017

Tumor-Mutational Burden



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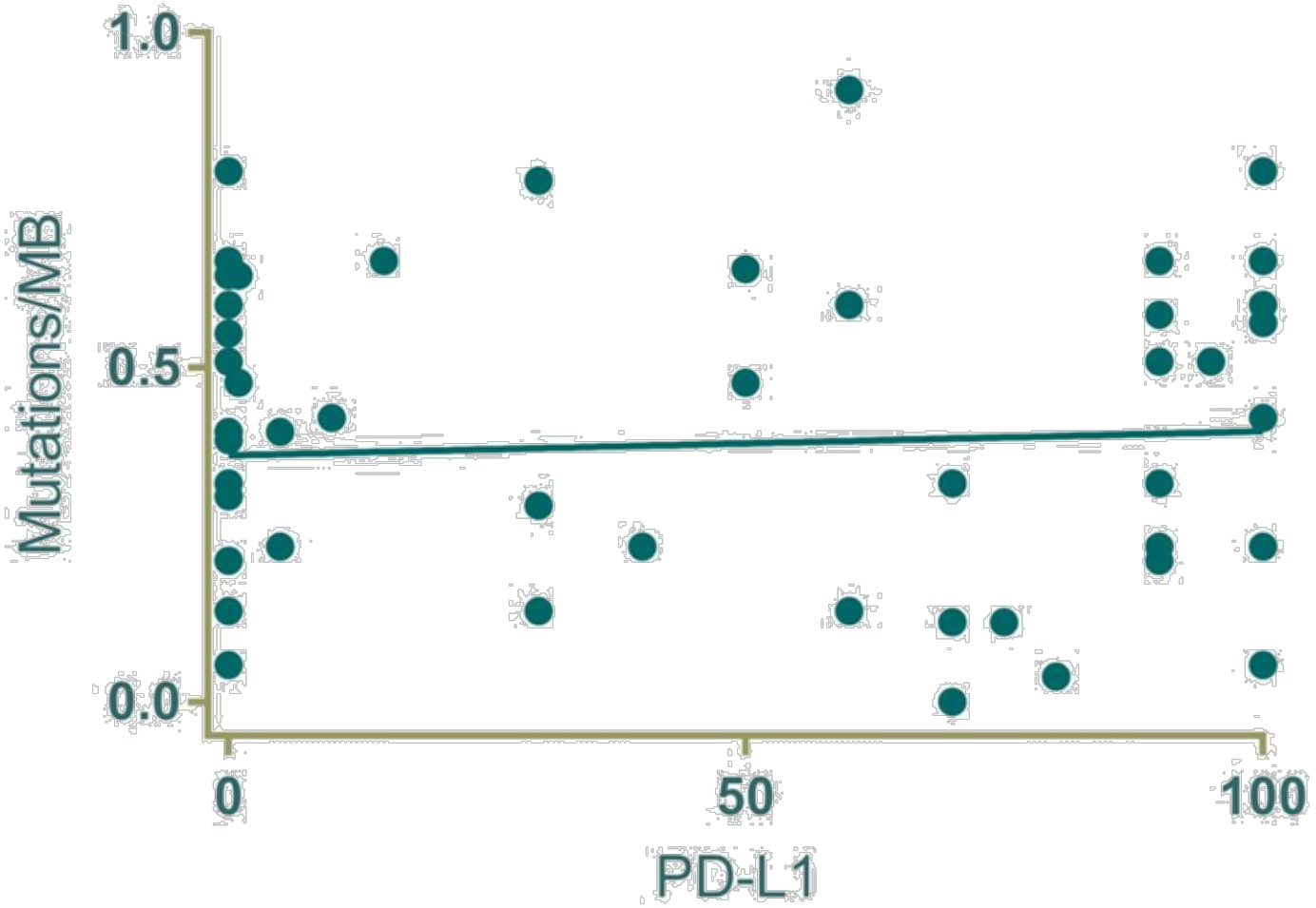
Sabari et al.; Abstr. 8512; ASCO 2017

Korrelation mit PD-L1



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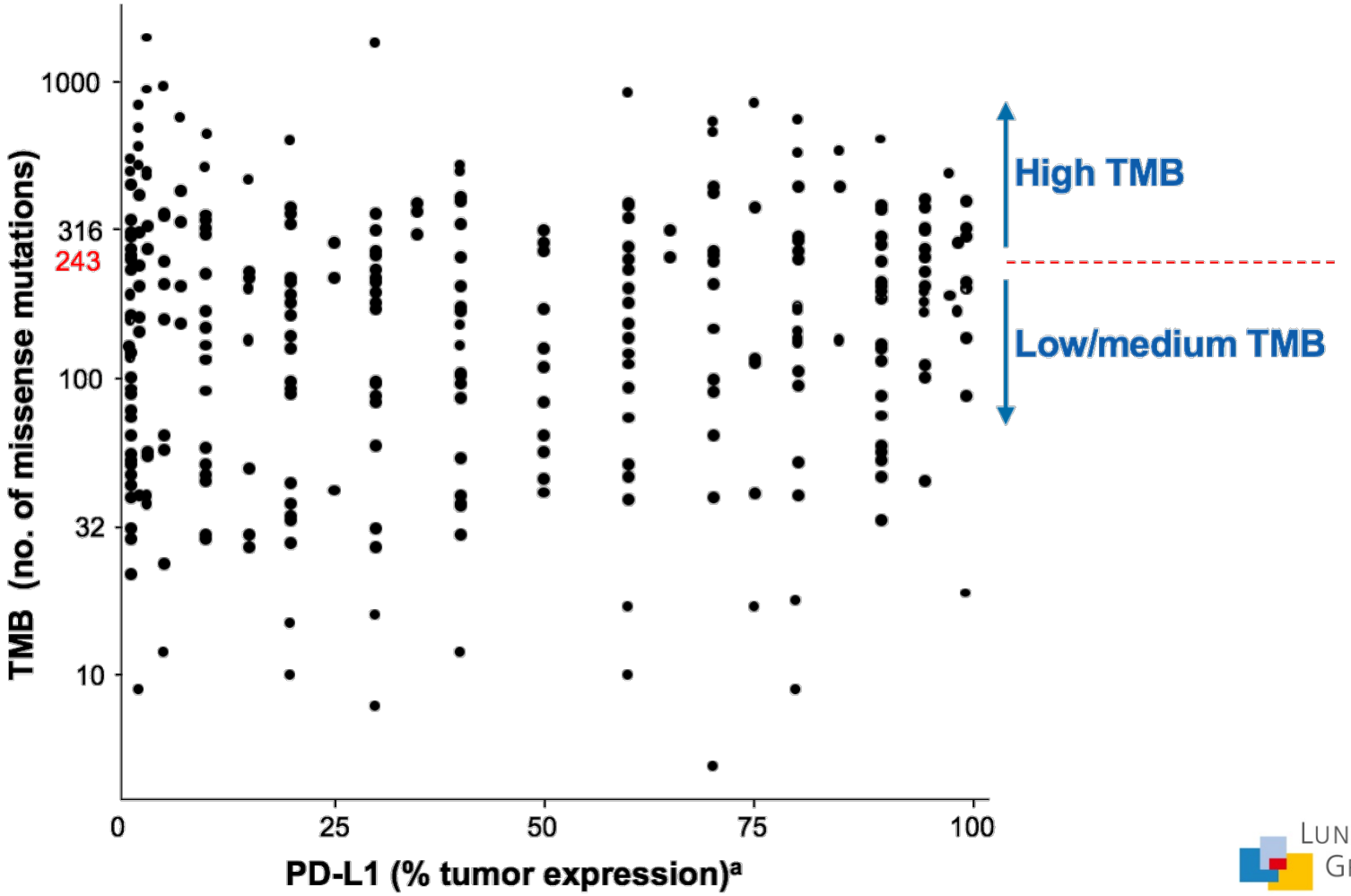
Sabari et al.; Abstr. 8512; ASCO 2017

Auch in Checkmate 26 keine Korrelation zwischen PD-L1 und TMB



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Peters, S., AACR 2017

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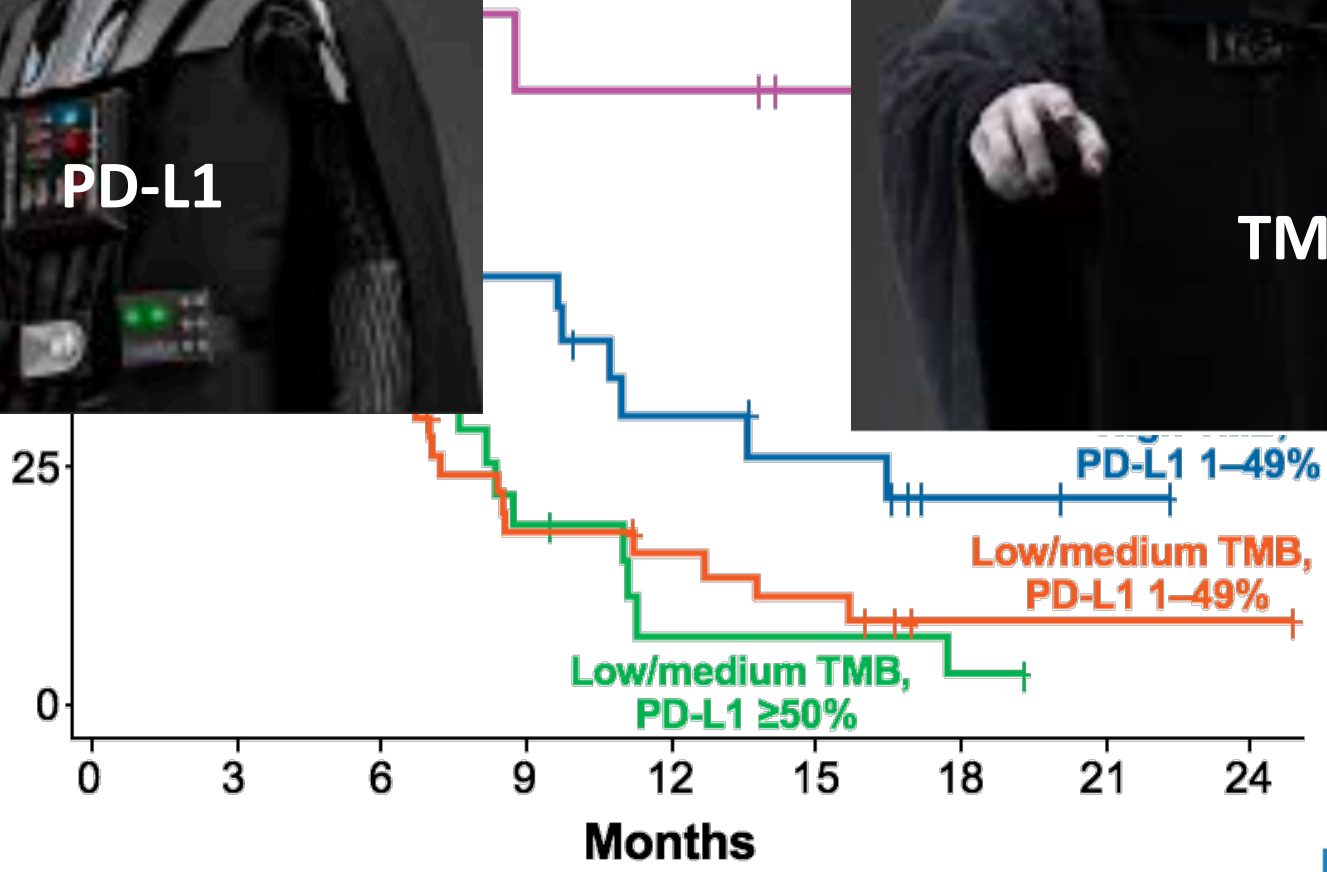

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Peters, S., AACR 2017, Lucasarts ©

Take Home MET und PD-1

- **MET-**Exon 14: **Treibermutation** in **3%** aller NSCLC (ungefähr=Inzidenz CML)
- Viel versprechende **ÜL**-Daten mit **MET**-Inhibitoren (z.B. **Crizotinib**)
- **PD-1 Inhibition** hilft **nicht**, **unabhängig** vom **PD-L1** Status.
- **TMB** generell der **bessere Prädiktor**

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Alectinib vs crizotinib in treatment-naïve advanced *ALK*+ NSCLC: primary results of the global phase III ALEX study (LBA9008)

Alice Shaw[1], Solange Peters[2], Tony Mok[3], Shirish M. Gadgeel[4], Jin Seok Ahn[5], Sai-Hong Ignatius Ou[6], Maurice Perol[7], Rafal Dziadziuszko[8], Dong-Wan Kim[9], Rafael Rosell[10], Ali Zeaiter[11], Ting Liu[11], Sophie Golding[11], Bogdana Balas[11], Johannes Noe[11], Peter N. Morcos[12], and D. Ross Camidge[13] on behalf of the ALEX investigators

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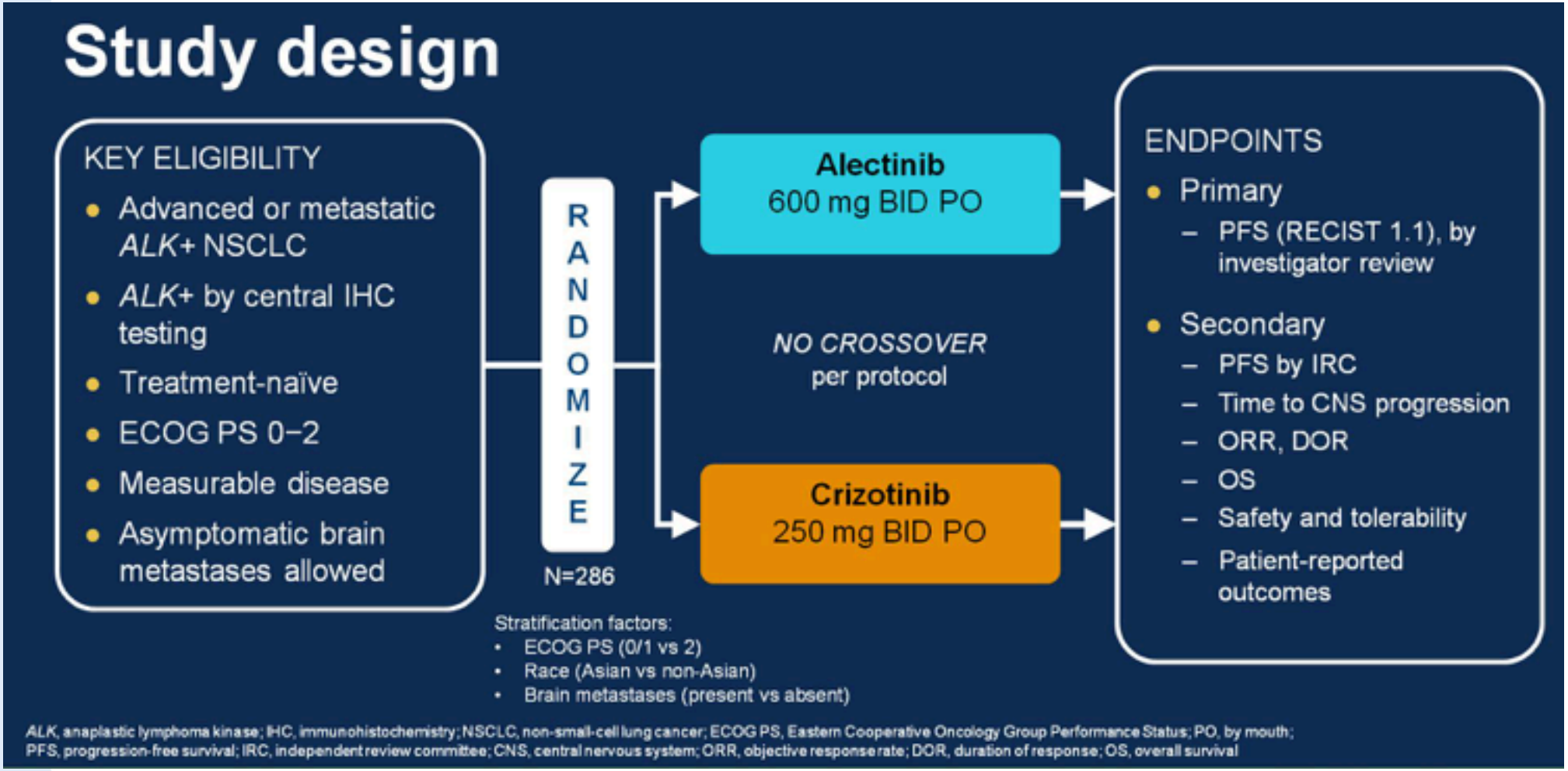
Shaw et al.; LBA9008; ASCO 2017

Study design



ALK, anaplastic lymphoma kinase; IHC, immunohistochemistry; NSCLC, non-small-cell lung cancer; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PO, by mouth; PFS, progression-free survival; IRC, independent review committee; CNS, central nervous system; ORR, objective response rate; DOR, duration of response; OS, overall survival

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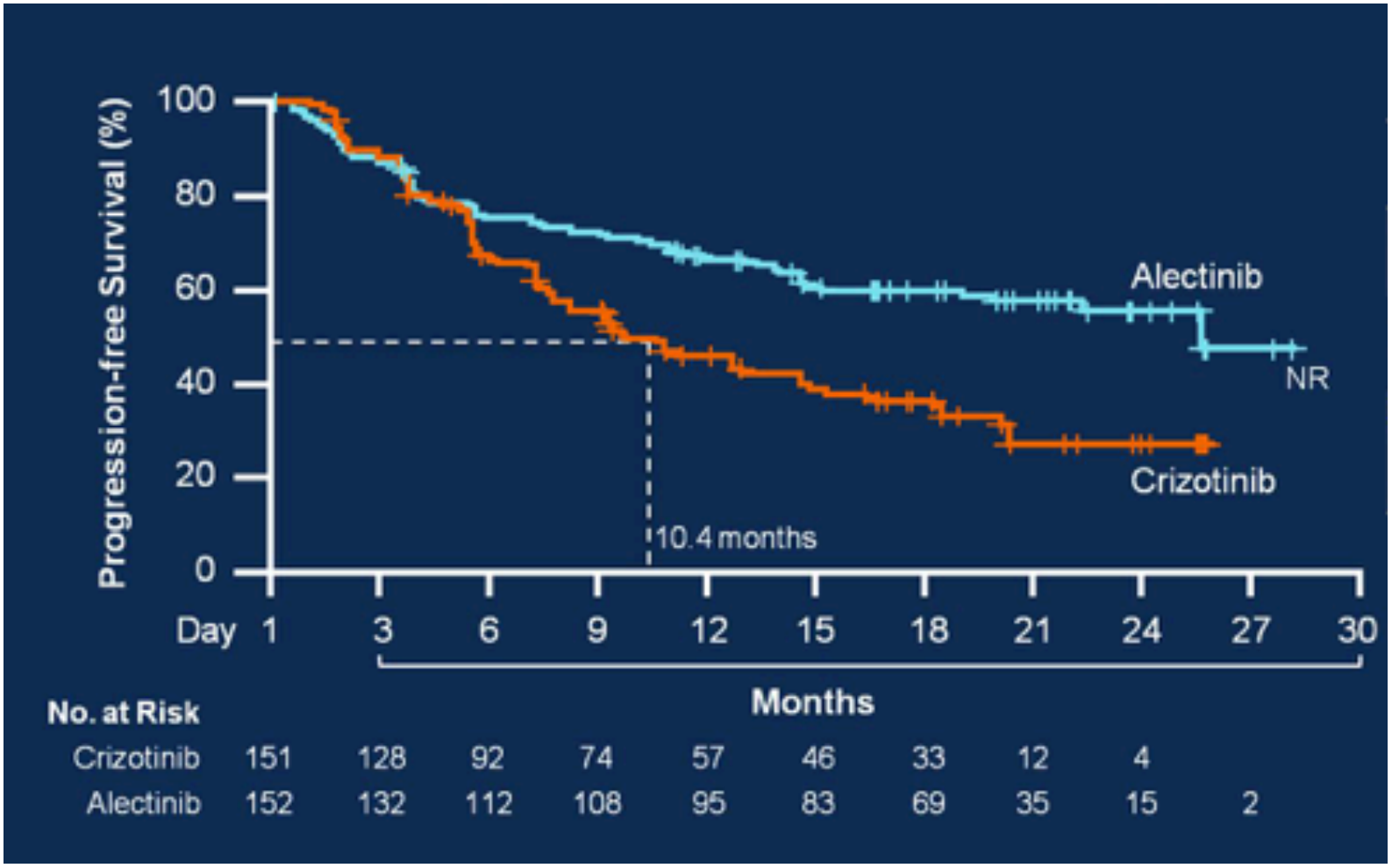
Shaw et al.; LBA9008; ASCO 2017

Endpunkt PFS (unabhängige, zentrale Beurteilung)



PFS 25,7 vs. 10,4 Monate (HR 0,5; p<0,0001

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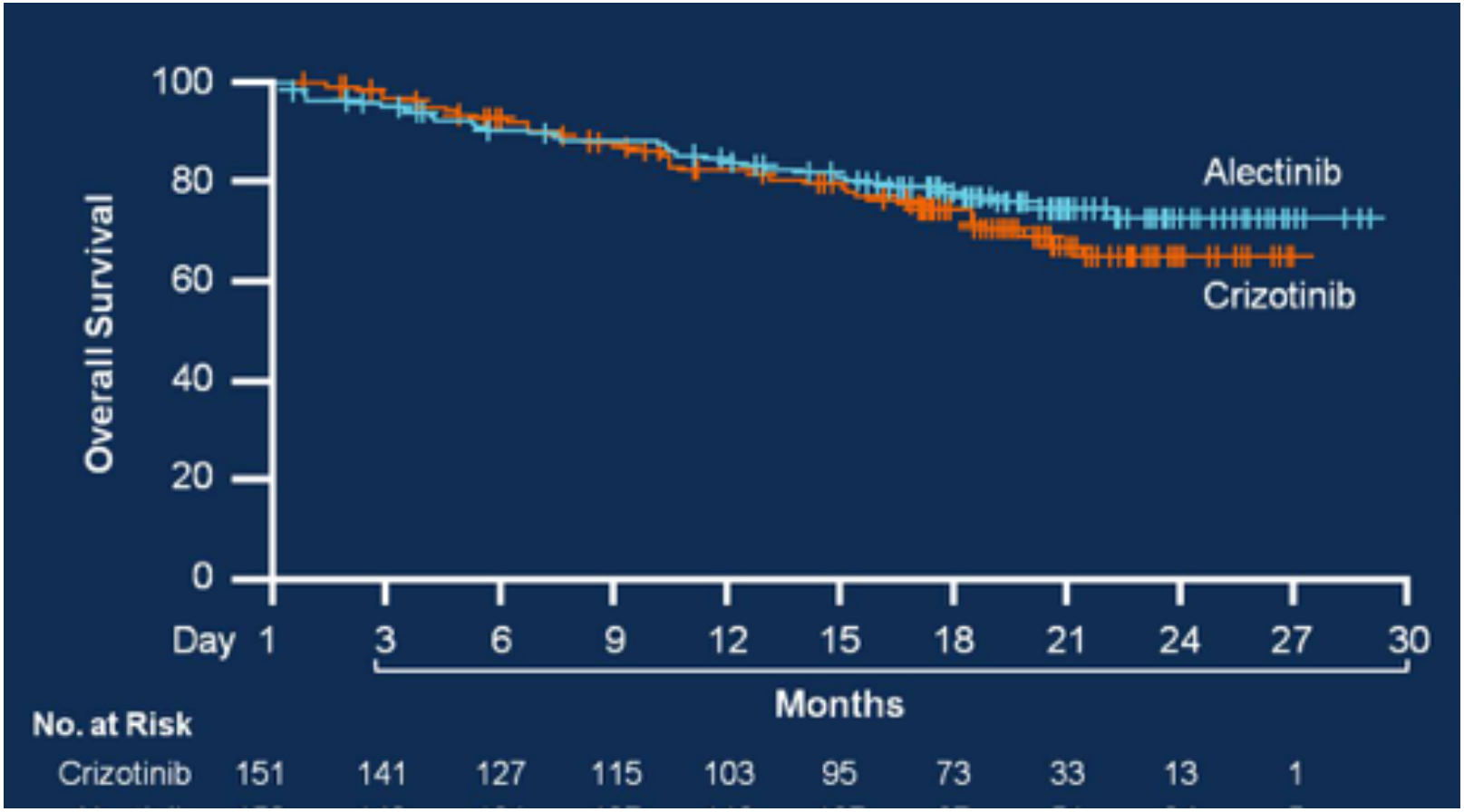
Shaw et al.; LBA9008; ASCO 2017

Gesamtüberleben noch (lange) nicht auswertbar



Im Crizo-Arm 27%, Im Alectinib-Arm 23% bisher verstorben

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Shaw et al.; LBA9008; ASCO 2017

...bei besserer Verträglichkeit

Adverse events, ≥10% between treatment arms

	Crizotinib (N=151)		Alectinib (N=152)	
N (%)	Any grade	Grade 3–5	Any grade	Grade 3–5
Nausea	72 (48)	5 (3)	21 (14)	1 (1)
Diarrhea	68 (45)	3 (2)	18 (12)	0
Vomiting	58 (38)	5 (3)	11 (7)	0
Peripheral edema	42 (28)	1 (1)	26 (17)	0
Dysgeusia	29 (19)	0	4 (3)	0
ALT increased	45 (30)	22 (15)	23 (15)	7 (5)
AST increased	37 (25)	16 (11)	21 (14)	8 (5)
Visual impairment	18 (12)	0	2 (1)	0
Blood bilirubin increased	2 (1)	0	23 (15)	3 (2)
Myalgia	3 (2)	0	24 (16)	0
Anemia	7 (5)	1 (1)	30 (20)	7 (5)
Weight increased	0	0	15 (10)	1 (1)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate transaminase

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Shaw et al.; LBA9008; ASCO 2017

Take Home Alectinib

- In puncto **PFS** mehr als **doppelt** so gut wie Crizotinib (**Xalkori ®**)
- **Überleben** noch **nicht beurteilbar,** aber Trend **zugunsten** Alectinib

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Geschafft!

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