

TOPICS IN LUNG CANCER

Lore Decoster, Medical Oncology, UZ Brussel

☰ Overview

1. Introduction

2. Metastatic NSCLC

- Metastatic NSCLC before 2018
- Novelties in targeted therapies
- Novelties in immunotherapy

3. Locally advanced NSCLC

4. Immunotherapy in advanced SCLC

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2. Metastatic NSCLC

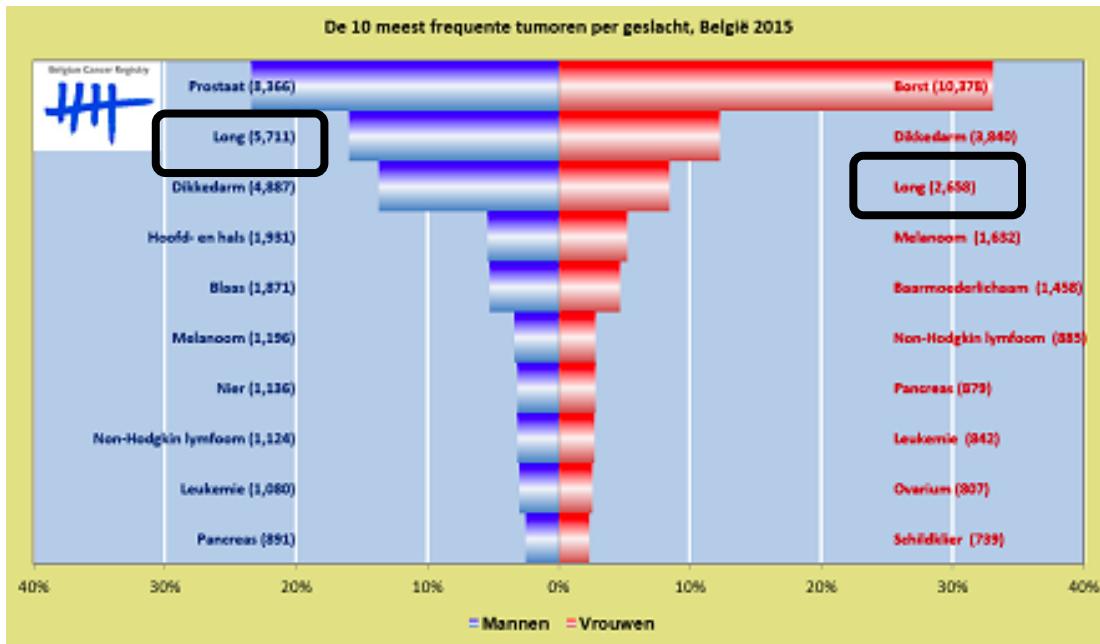
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III Introduction

8000 new cases /y in Belgium



Introduction

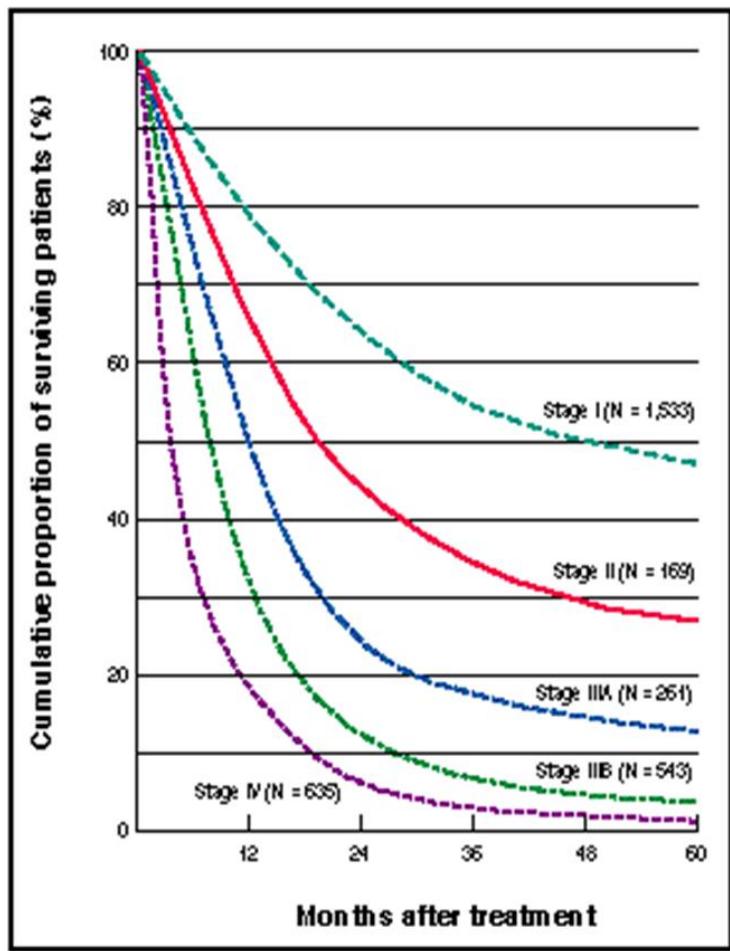
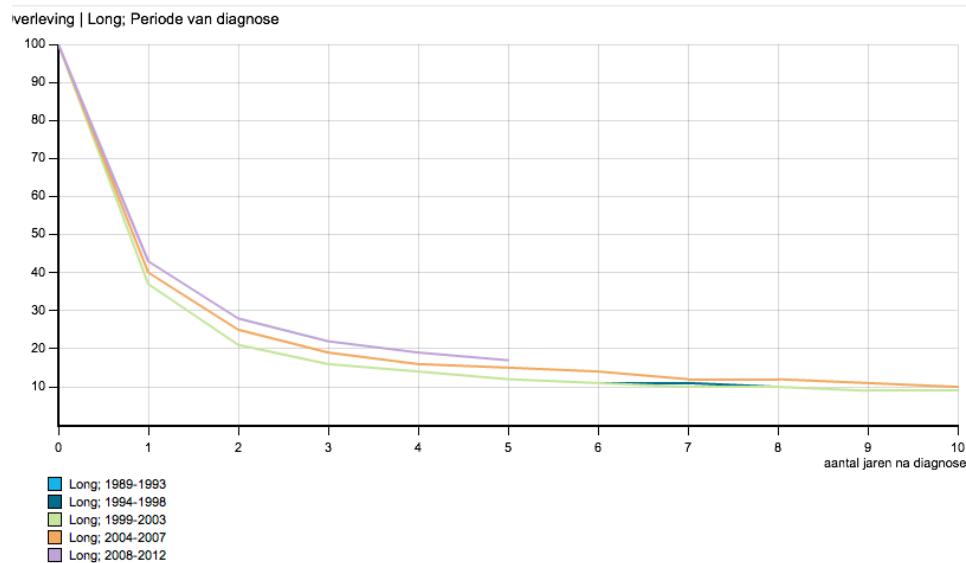


Figure 3. Survival rates after surgical resection by stage of disease ($P < .001$).

Adapted from Mountain (10).



www.cijfersoverkanker.nl

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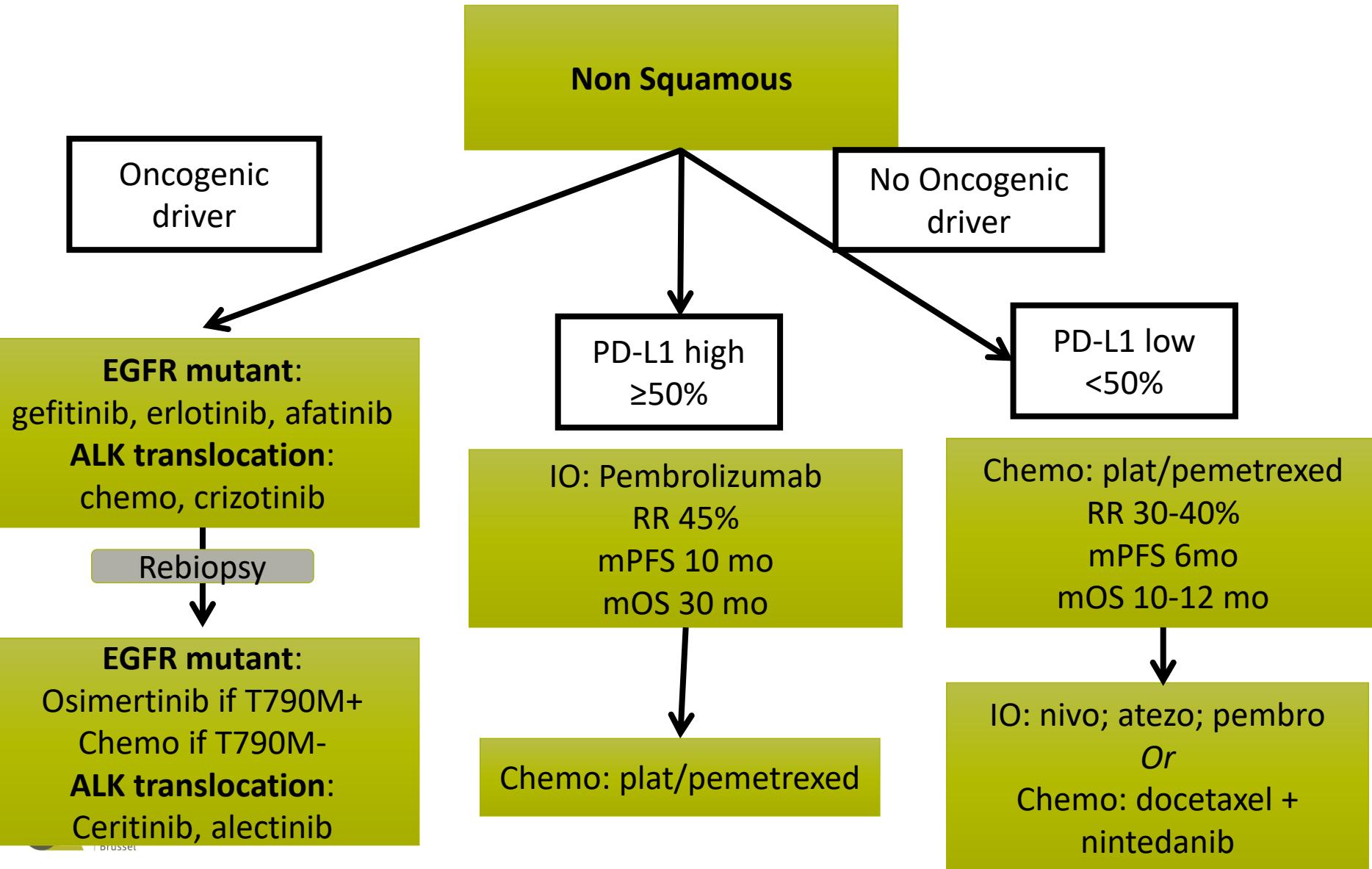
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- Novelties in immunotherapy

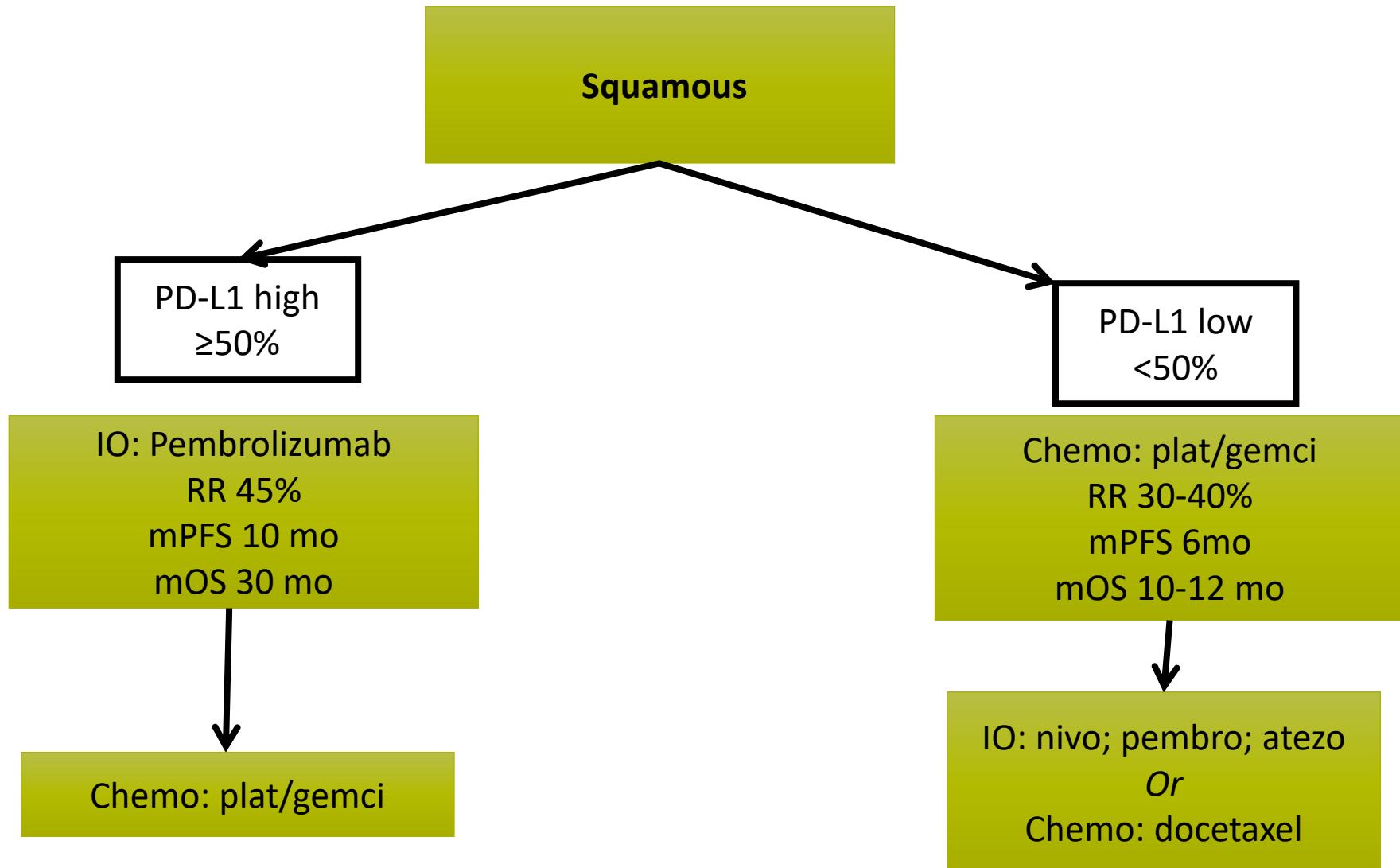
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NSCLC before 2018



NSCLC before 2018



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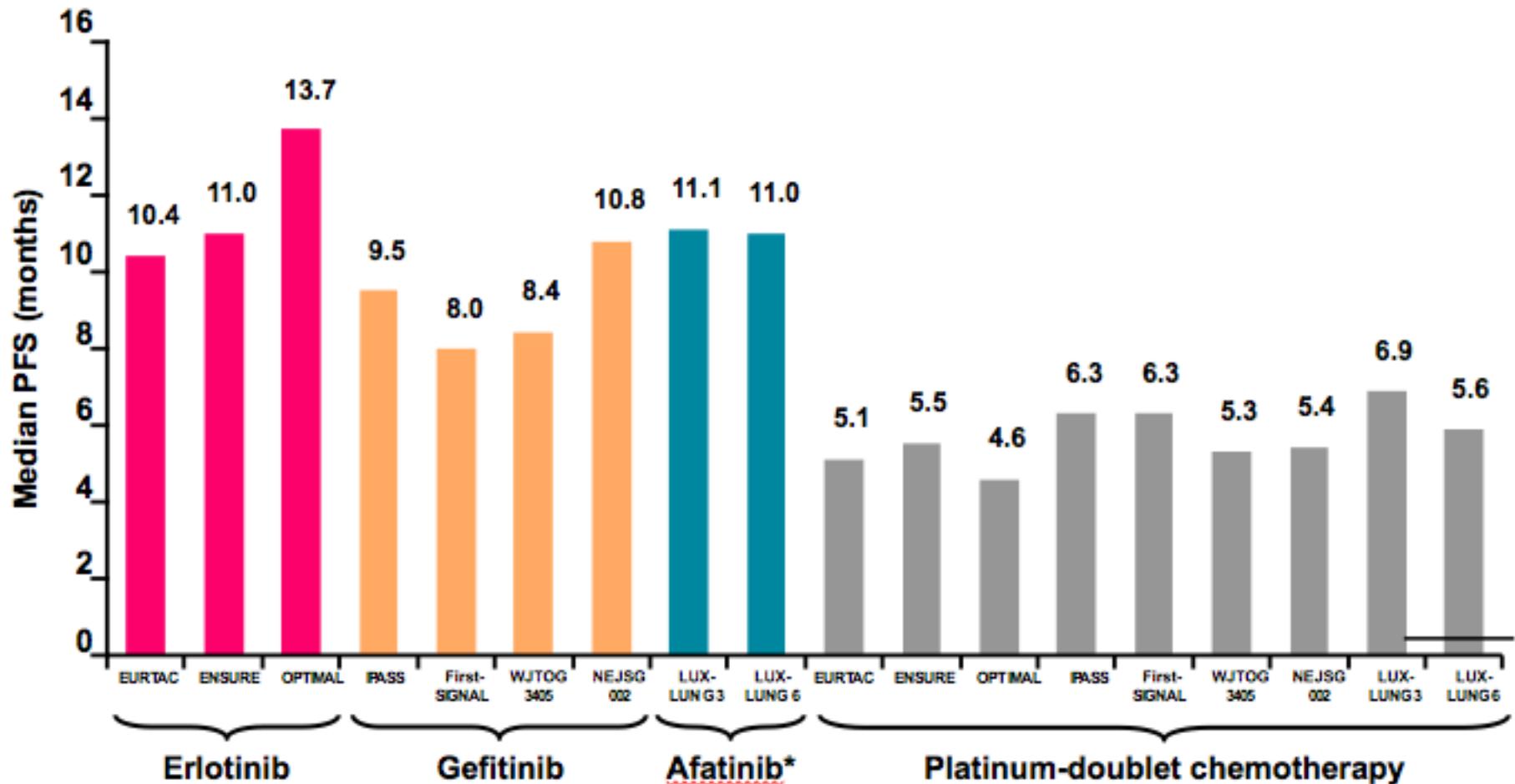
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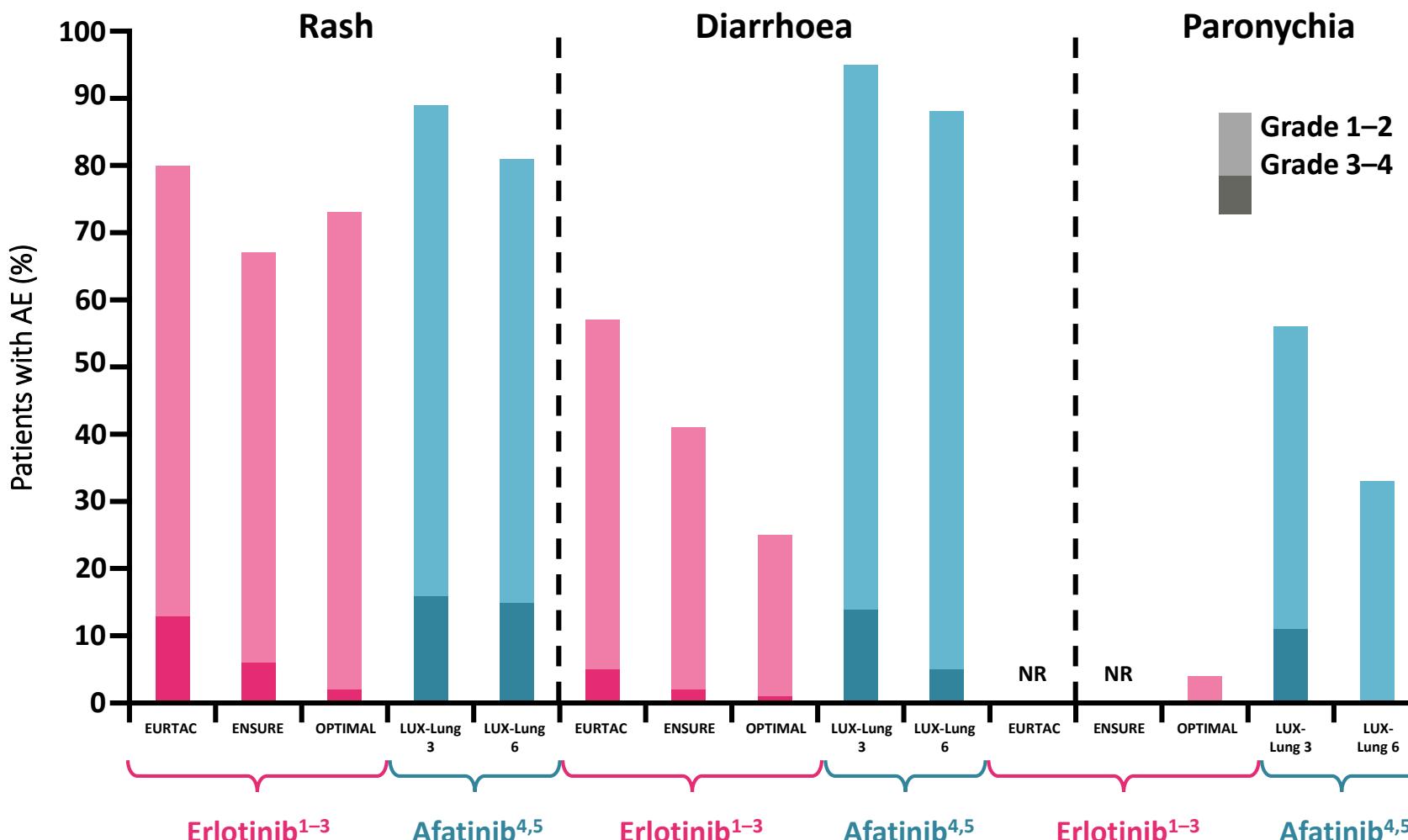
EGFR mutant NSCLC (+/- 10%)



Cross-trial comparison. Data should be interpreted with caution
*All EGFR mutations
PFS = progression-free survival

* Costa, et al. Clin Cancer Res 2014; Wu, et al. WCLC 2013, Chen, et al. Ann Oncol 2013; Gefitinib SmPC 2010; Han, et al. J Clin Oncol 2012, Mitsuhashi, et al. Lancet Oncol 2010; Maemondo, et al. N Engl J Med 2010, Sequist, et al. J Clin Oncol 2013; Wu, et al. Lancet Oncol 2014

EGFR mutant NSCLC

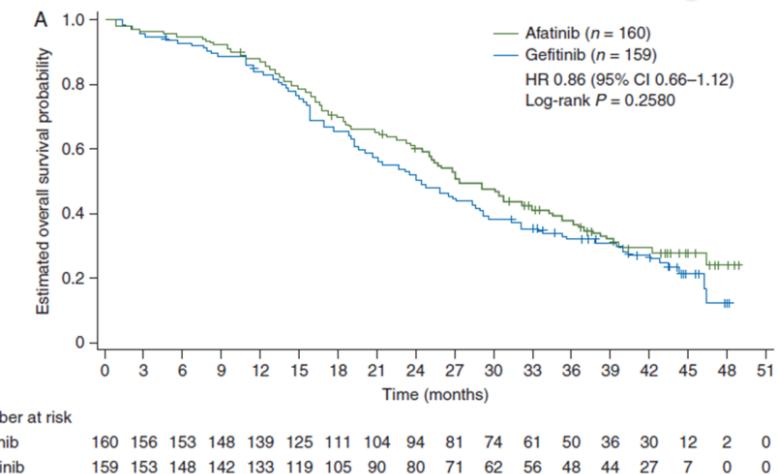
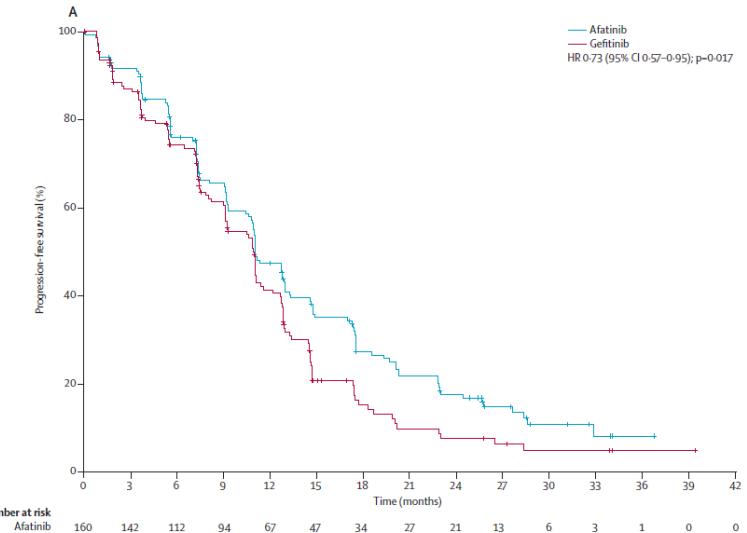


1. Rosell, et al. *Lancet Oncol* 2012; 2. Wu, et al. *WCLC* 2013
3. Zhou, et al. *Lancet Oncol* 2011; 4. Sequist, et al. *J Clin Oncol* 2013; 5. Wu, et al. *Lancet Oncol* 2014

2nd vs 1st generation TKI

Lux-Lung7: phase 2 afatinib vs gefitinib

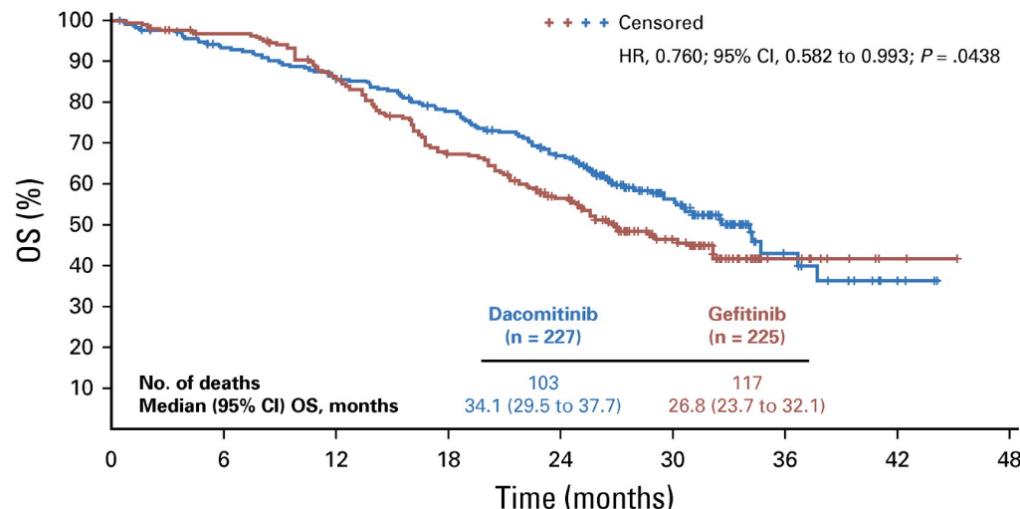
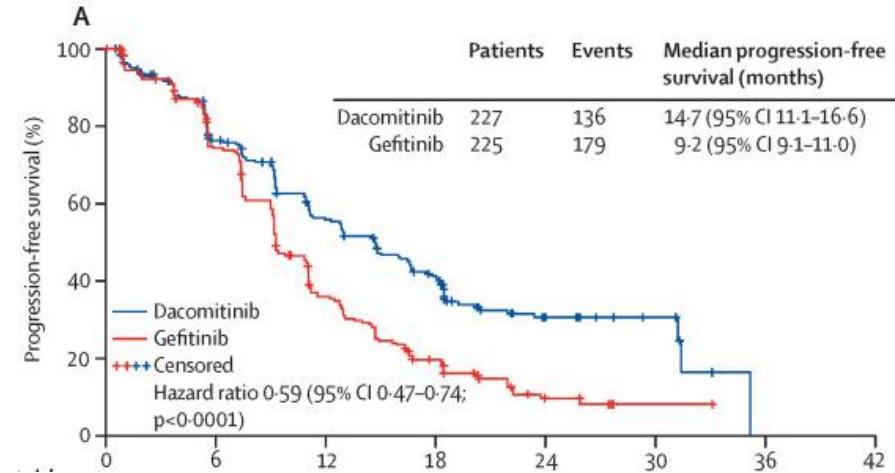
- RR 70 vs 56%; p=0.008
- mPFS 11 vs 10.9 mo;
HR 0.73; p=0.007
- mOS 27.9 vs 24.5 mo ;
HR 0.86; p=0.26



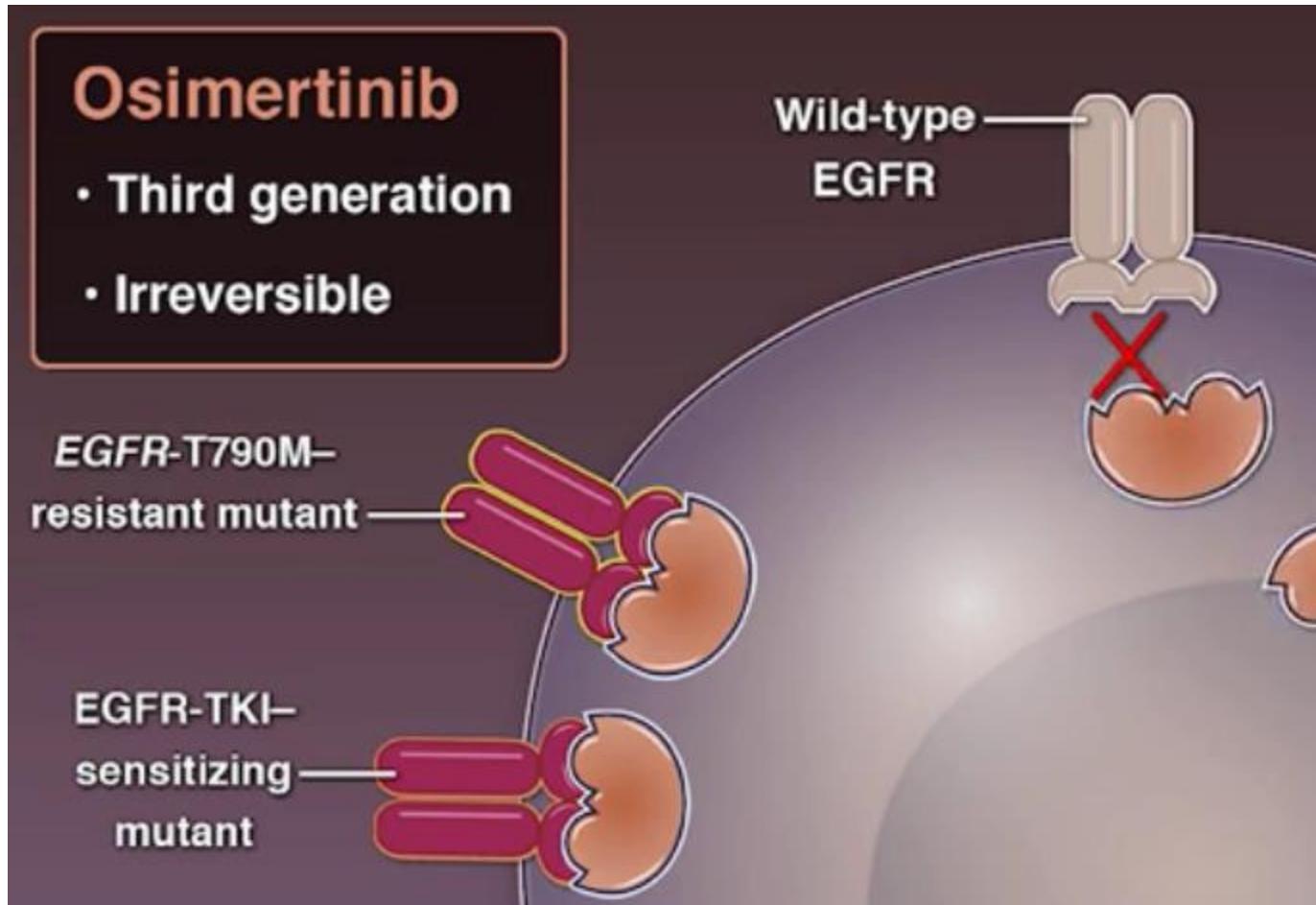
2nd vs 1st generation TKI

ARCHER 1050: phase 3 dacomitinib vs gefitinib

- RR 75 vs 72 p=0.42
- mPFS 14.7 vs 9.2;
HR 0.59; p<0.001
- mOS 43 vs 27;
HR 0.76; p=0.04
- More G3/4 AE ;
more diarrhea



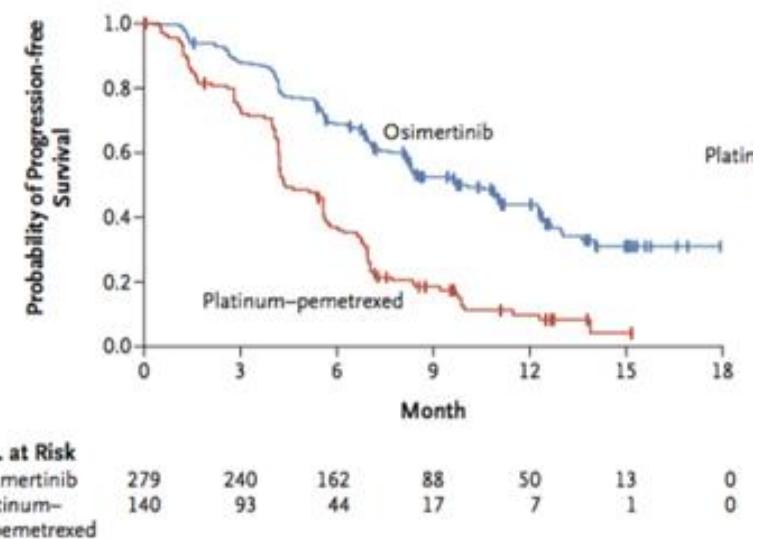
„ 3rd generation EGFR TKI: osimertinib



III 3rd gen TKI: Osimertinib

AURA-3 studie 2nd line if T790M vs chemo

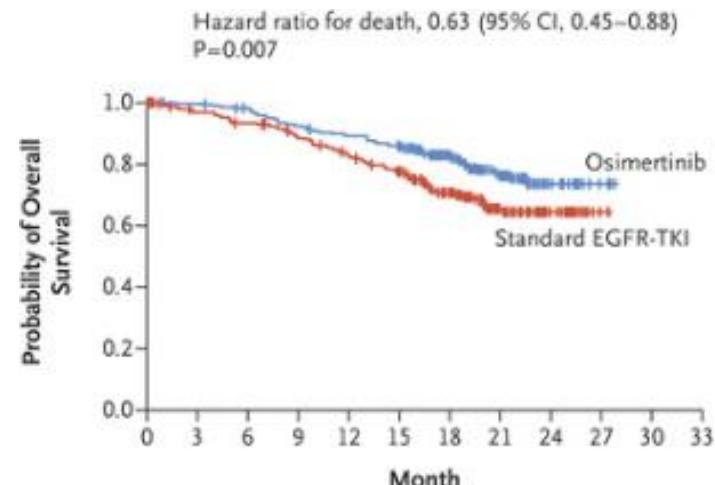
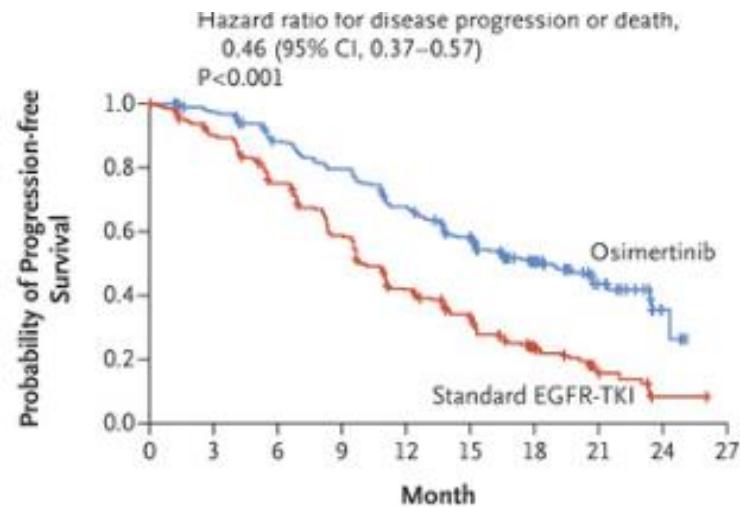
- RR 71 vs 31%; p<0.001
- PFS 10.1 vs 4.4 mo;
HR 0.30; p<0.001



III 3rd gen TKI: Osimertinib 1st line

FLAURA: phase 3 osimertinib vs gefitinib/erlotinib

- RR 80 vs 76%; p=0.24
- mPFS 18.9 vs 10.2 mo;
HR 0.46; p<0.001
- mOS immature
HR for death 0.63

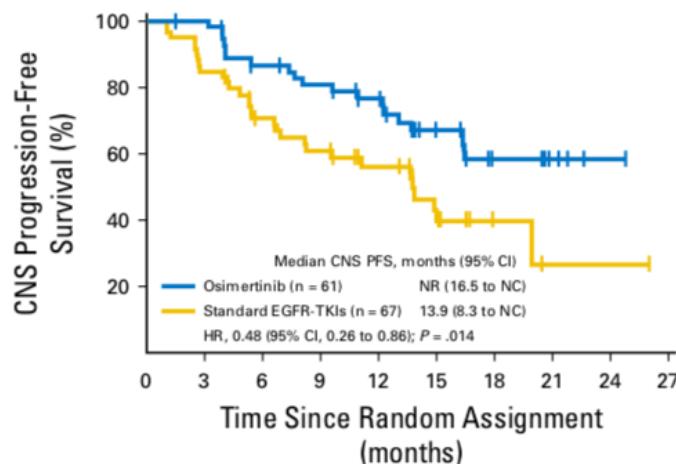


3rd gen TKI: Osimertinib 1st line

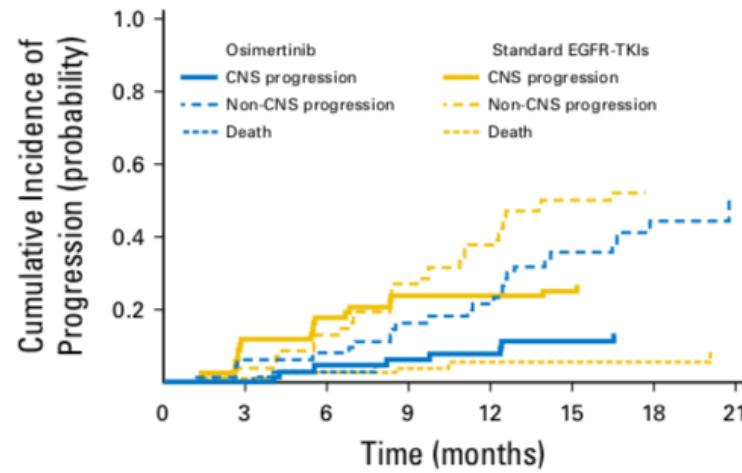
➤ Sub-analysis of brainM+ in FLAURA

- ICR 91% vs 68% ($p=0.066$)
- Median CNS PFS NR vs 13.9 mo (HR 0.48; $p=0.14$)
- Lower probability of CNS progression: 24 vs 35% at 1y

A



C

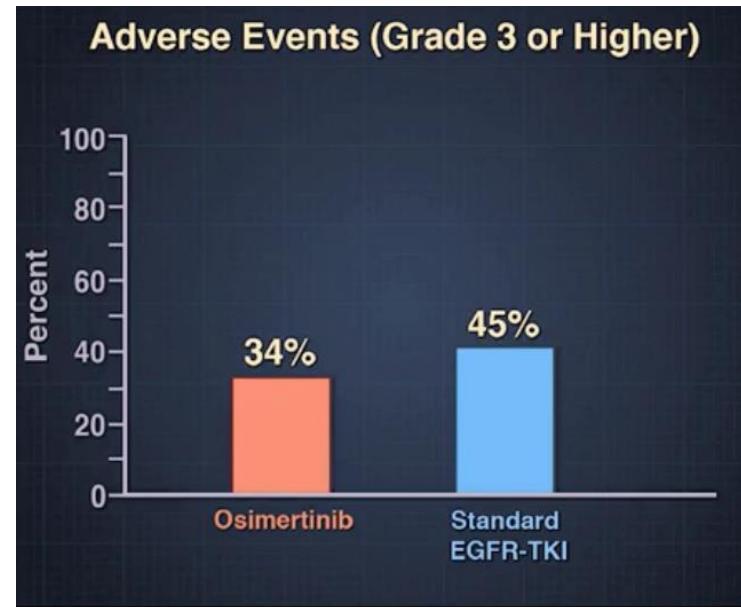


No. at risk:

Osimertinib	61	54	44	40	34	21	8	4	1	0
Standard EGFR-TKIs	67	50	37	31	21	13	4	1	1	0

3rd gen TKI: Osimertinib 1st line

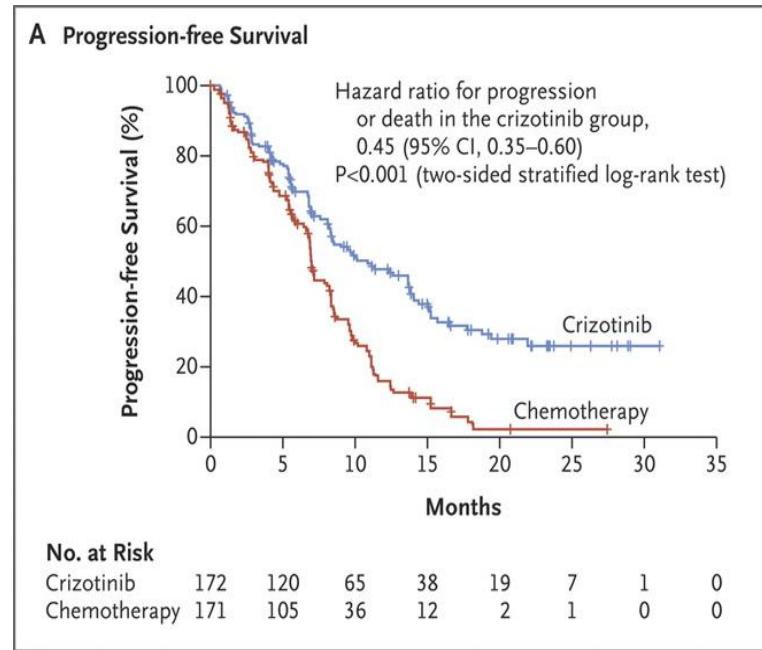
- Less grade 3/4 toxicity
- Rash all grade 58 vs 78%
- Similar all grade diarrhea 58 vs 57%



ALK translocated NSCLC (5%)

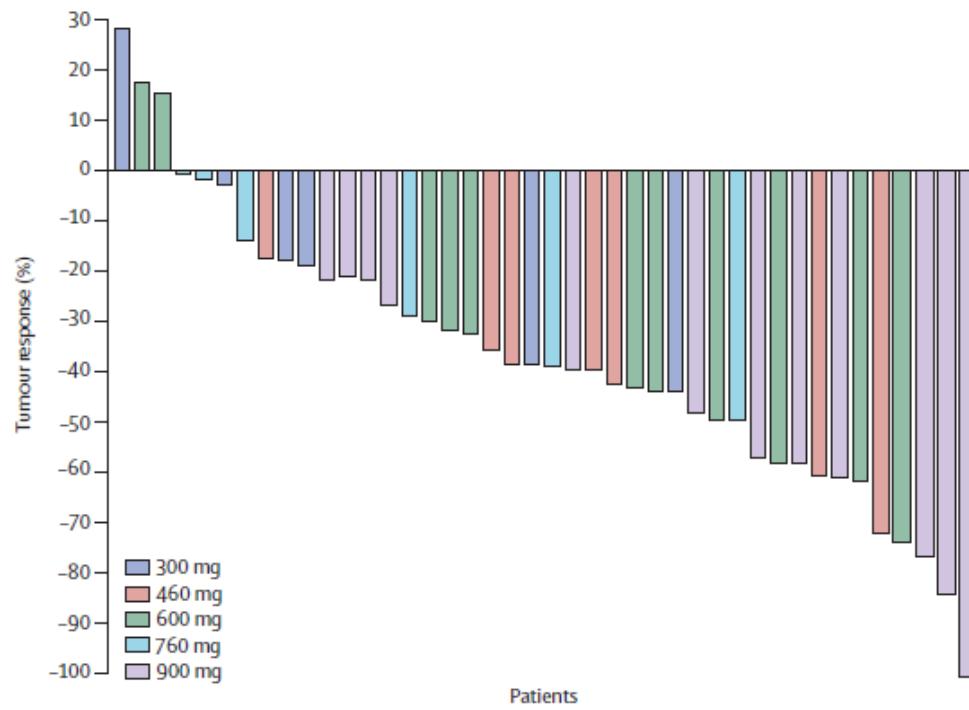
PROFILE 1014 Crizotinib 1st line

- ORR 74% vs 45%
- PFS 10.9 vs 7 mo
HR 0.45; p<0.001
- HR for death 0.82



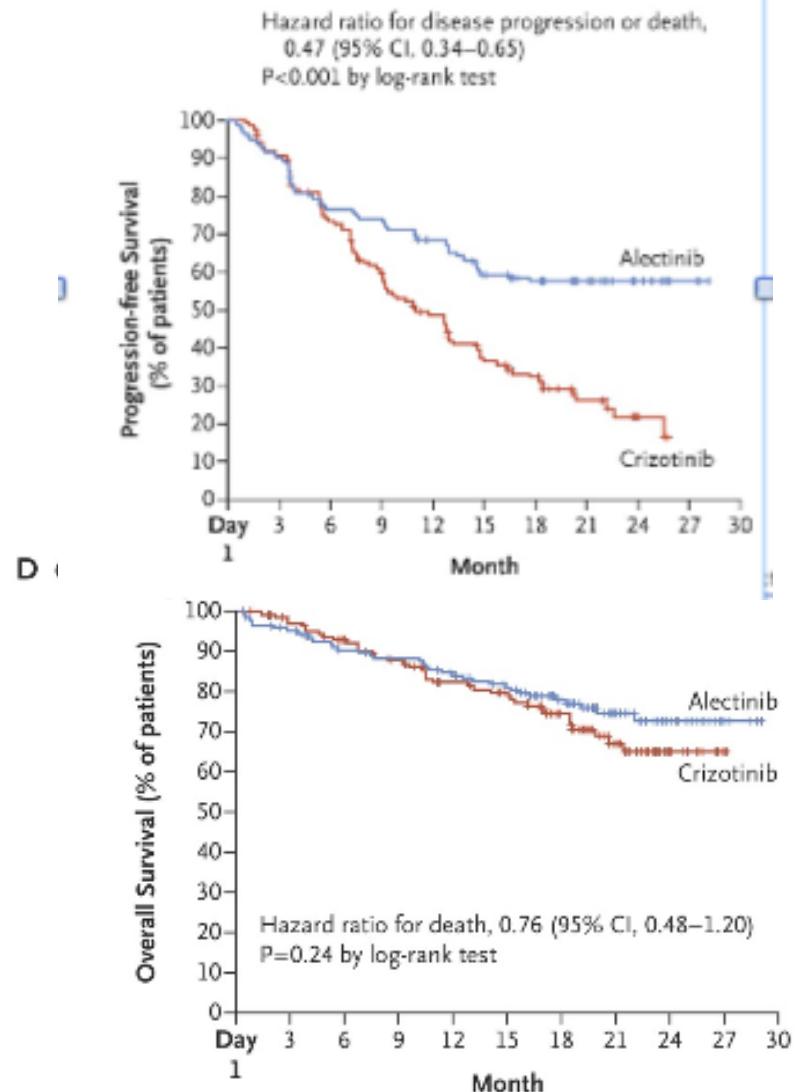
☰ Alectinib after crizotinib

- RR 55%
- 52% respons in CNS



III ALEX: Alectinib vs crizotinib

- RR 82,9 vs 75,5; p=0.09
- mPFS NR vs 11 mo;
HR 0.47; p<0.001
- OS immature;
HR for death 0.76

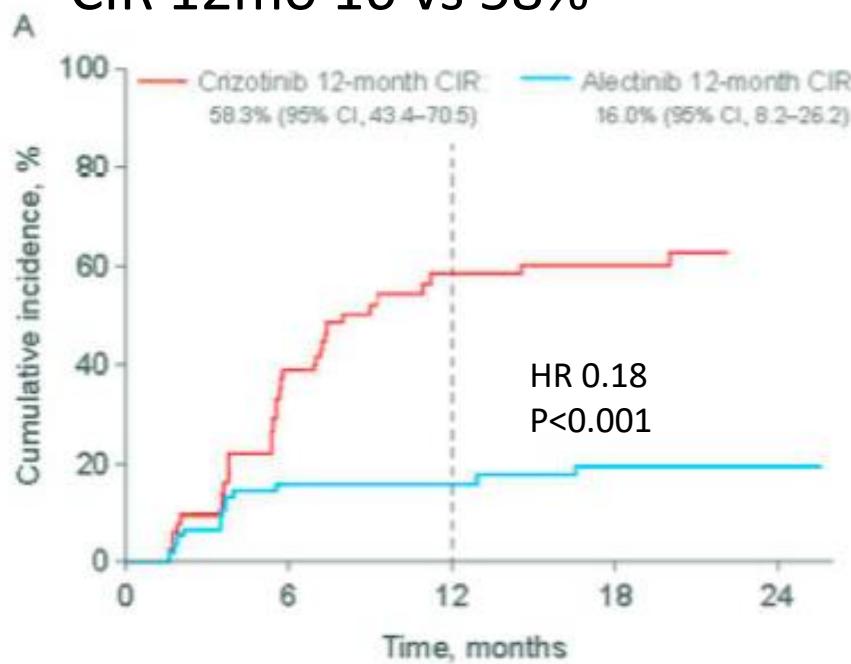


ALEX: Alectinib vs crizotinib 1st line

Alectinib delays CNS progression vs crizotinib

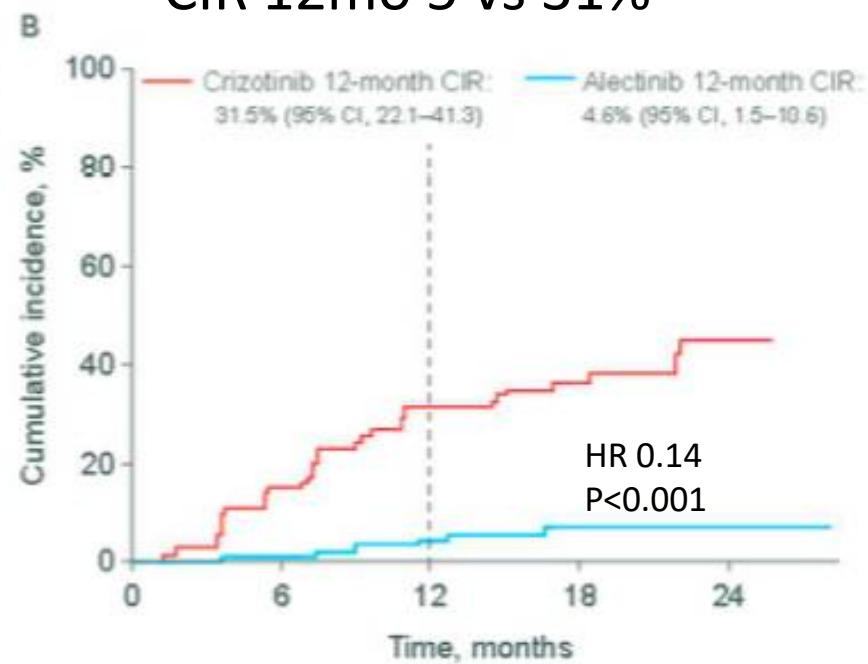
Baseline CNS M+

CIR 12mo 16 vs 58%



No baseline CNS M+

CIR 12mo 5 vs 31%

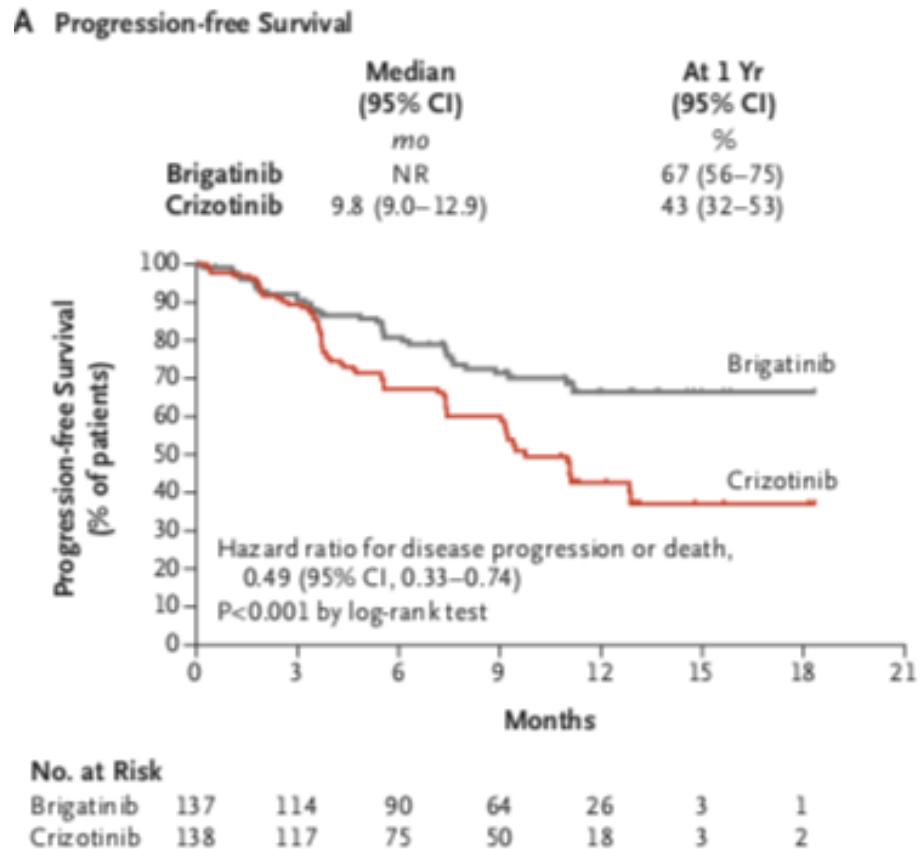


III ALEX: Alectinib vs crizotinib 1^e lijn

- Less AE grade 3/5: 41 vs 50%
- Less Gastrointestinal and visual AE
 - Nausea 14 vs 48%
 - Diarrhea 12 vs 45%
 - Vomiting 7 vs 38%
 - Visual 1 vs 12%
- More myalgia (16 vs 2%);
photosensitivity (5 vs 0%) and anemia
(20 vs 1%)

Brigatinib vs crizotinib 1st line ALTA-1L

- ORR 71 vs 60%
- mPFS NR vs 9.8 mo
 - HR 0.49; p<0.001
 - 12mo PFS 67 vs 43%
- OS immature

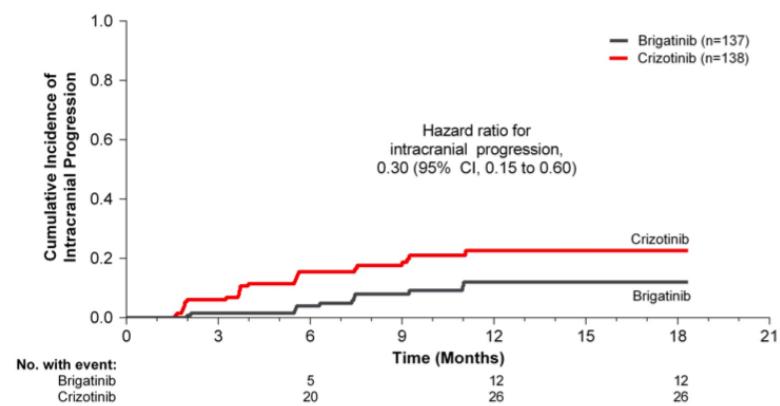
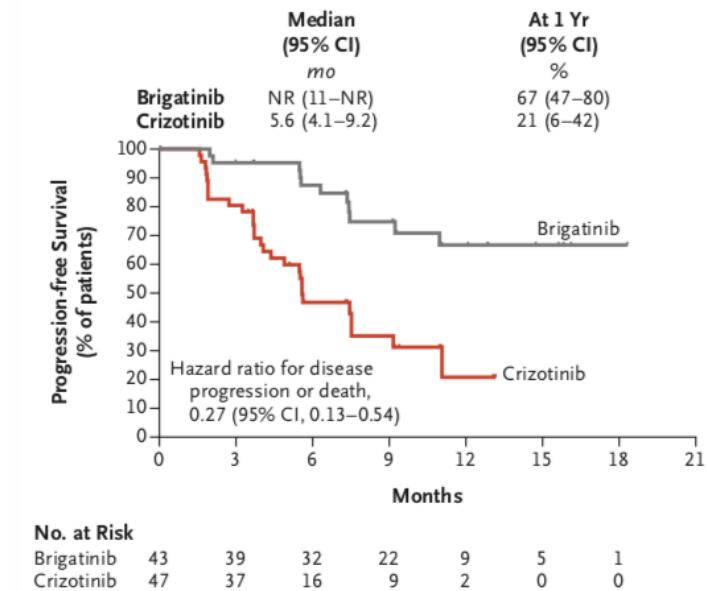


Camidge et al. *N Eng J Med* 2018

Brigatinib vs crizotinib 1st line ALTA-1L

- ICR 78 vs 50%
- Longer mPFS in brainM+
- Lower cumulative incidence
Of intracranial progression

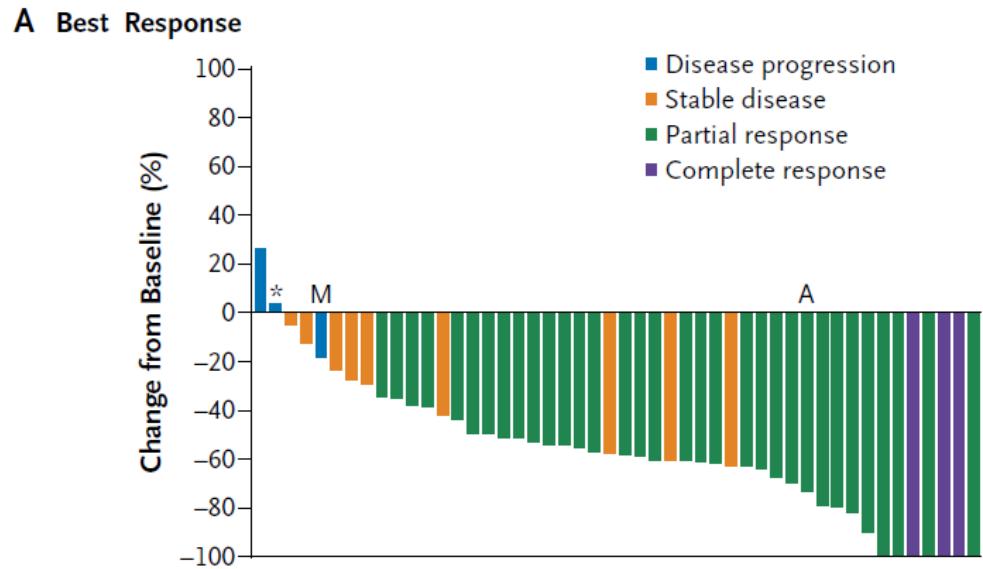
D Survival without Intracranial Disease Progression among Patients with Brain Metastases at Baseline



Camidge et al. *N Eng J Med* 2018

NSCLC ROS1 translocation (1-2%)

- Crizotinib:
 - RR 72%
 - PFS 19.2 mo
 - 1yOS 85%



Bergethon et al. *J Clin Oncol* 2012; Shaw et al. *N Eng J Med* 2014

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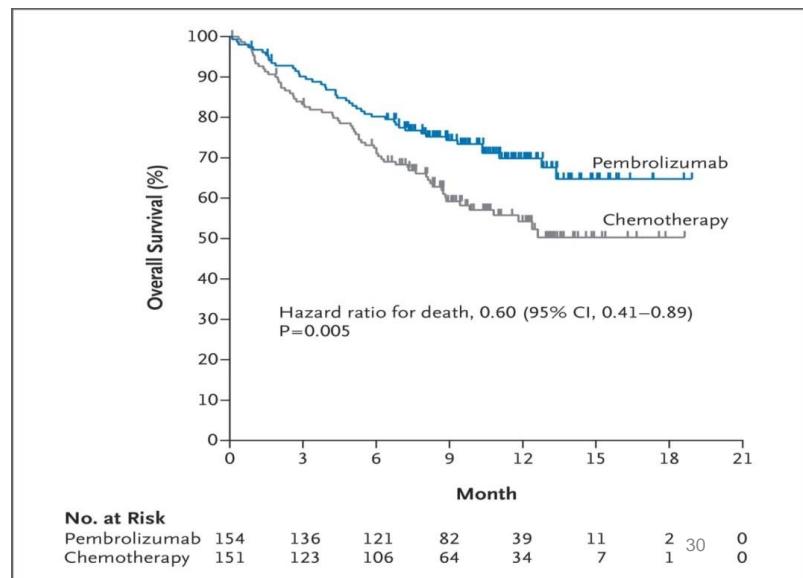
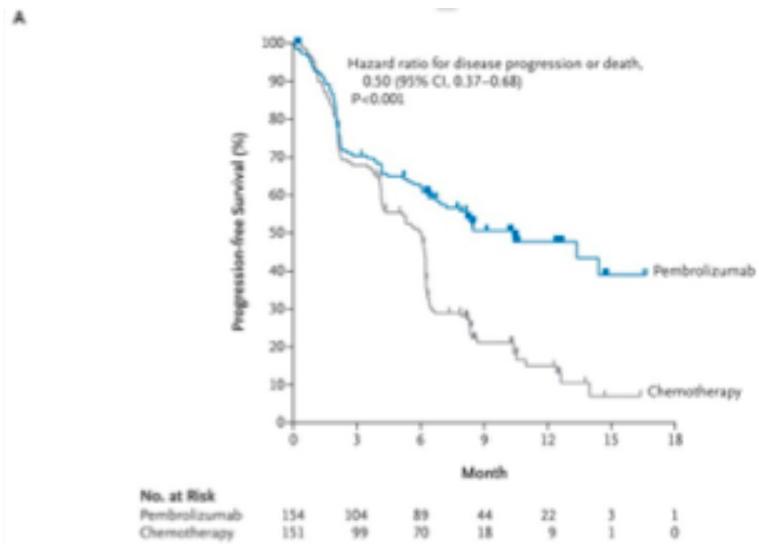
4. Immunotherapy in advanced SCLC

NSCLC: 2^e line anti-PD(L)1

Study	Checkmate-017 Nivolumab vs docetaxel	Checkmate-057 Nivolumab vs docetaxel	Keynote-010 Pembrolizumab vs docetaxel	OAK Atezolizumab vs docetaxel
Histology	squamous	Non-squamous	all	all
PD-L1 selection	No	No	YES; ≥1%	No
Response	20 vs 9%	19 vs 12%	18 vs 9%	14 vs 13%
m duration response	NR vs 8.4 m	17.2 vs 5.6 m	NR	16.3 vs 6.2 m
mPFS	3.5 vs 2.8 m	2.3 vs 4.3 m	3.9 vs 4 m	2.8 vs 4 m
1yPFS	21 vs 6%	19 vs 8%	NR	NR
mOS	9.2 vs 6 m; HR 0.59	12.2 vs 9.4; HR 0.72	10.4 vs 8.5 m; HR 0.71	13.8 vs 9.6m; HR 0.73
1y OS	42 vs 24%	51 vs 39%	43 vs 35%	NR

KEYNOTE-024: 1 st line Pembrolizumab in PD-L1 \geq 50% NSCLC

- RR 44.8 vs 27.8%
- mPFS 10.3 vs 6 mo;
HR 0.50; p<0.002
- mOS NR; H 0.60; p=0.005
- 6 mo OS 80% vs 72%

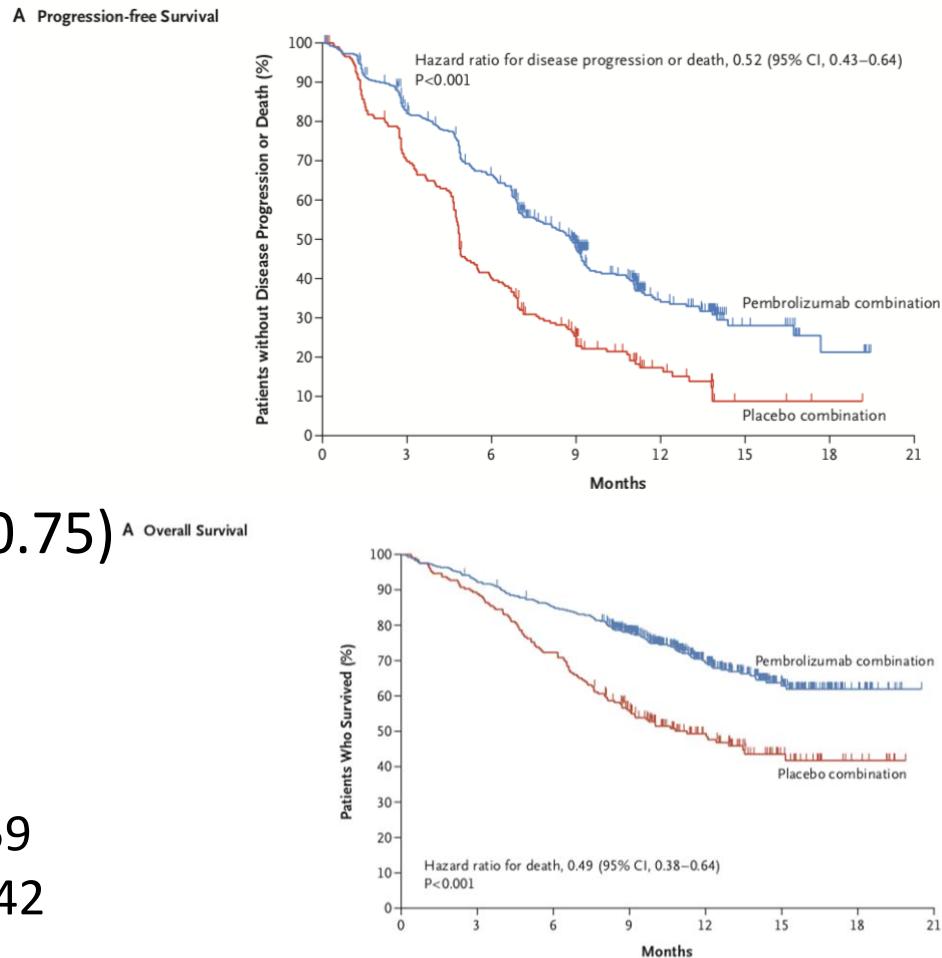


IO-Chemotherapy combinations in Non squamous NSCLC

- Keynote-189:
pembrolizumab/platinum/pemetrexed
- IMPower 150:
atezolizumab/avastin/carboplatin/paclitaxel
- IMPower 130:
atezolizumab/carboplatin/nabpaclitaxel
- IMPower 132:
atezolizumab/platinum/pemetrexed

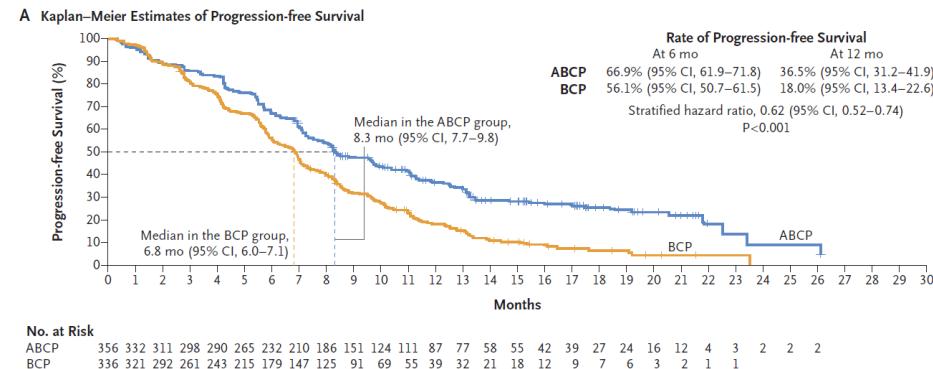
KEYNOTE-189: non Squamous: platinum/pemetrexed +/- pembrolizumab

- RR 47.6 vs 18.9%, p<0.001
- mPFS 8.8 vs 4.9 mo;
HR 0.52; p<0.001
(PDL1 neg: 6.1 vs 5.1 mo; HR 0.75)
- mOS NR vs 11.3 mo;
HR 0.49; p<0.001
 - PDL1 neg 1yOS 62 vs 52; HR 0.59
 - PDL1 high 1yOS 73 vs 48; HR 0.42

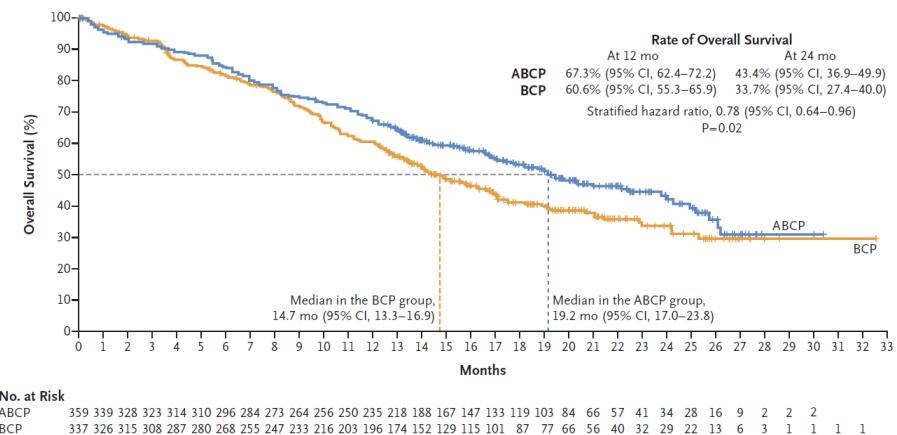


IMPower150: non Squamous: Atezo/beva/carbo/paclitaxel

- mPFS 8.3 vs 6.8 mo;
HR 0.62; p<0.0001

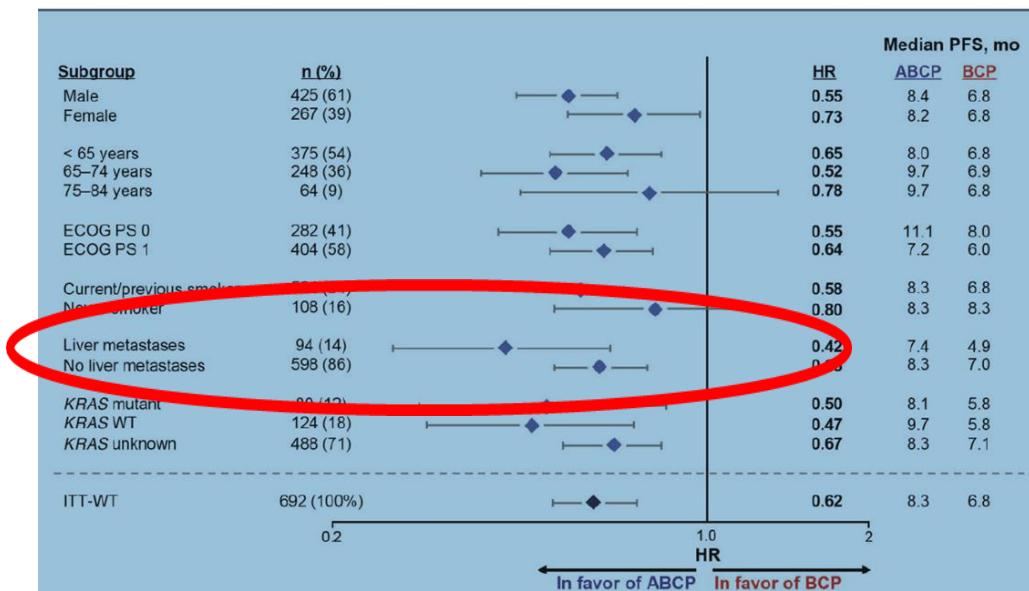
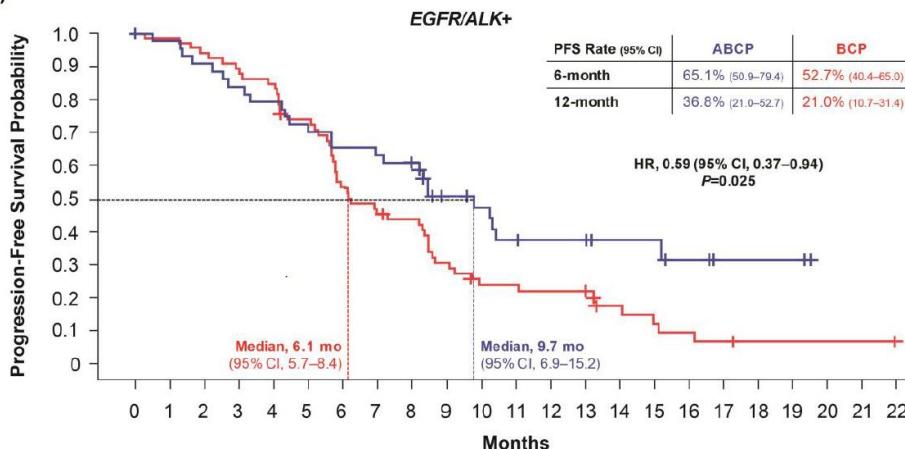


- mOS 19.2 vs 14.7 mo;
HR 0.78; p=0.02



IMPower150: Special populations

A)

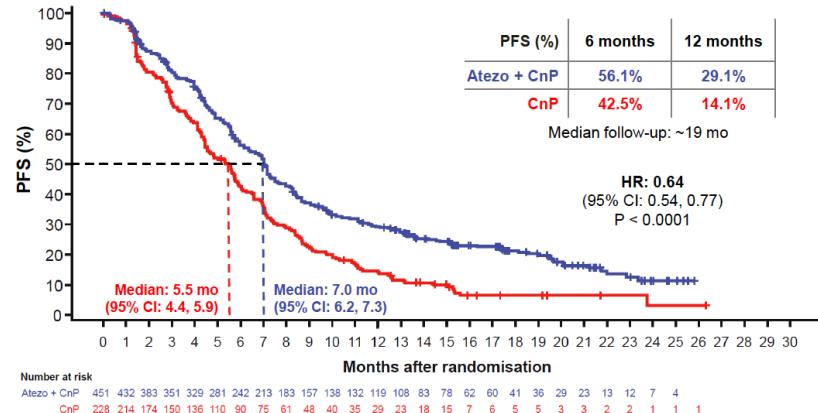


IMPower130: non Squamous Atezo + carboplatin/nabpaclitaxel

- RR 49 vs 32%
- mPFS 7 vs 5.5 mo;
HR 0.64; p<0.0001
- mOS 18.6 vs 13.9 mo;
HR 0.79; p=0.033

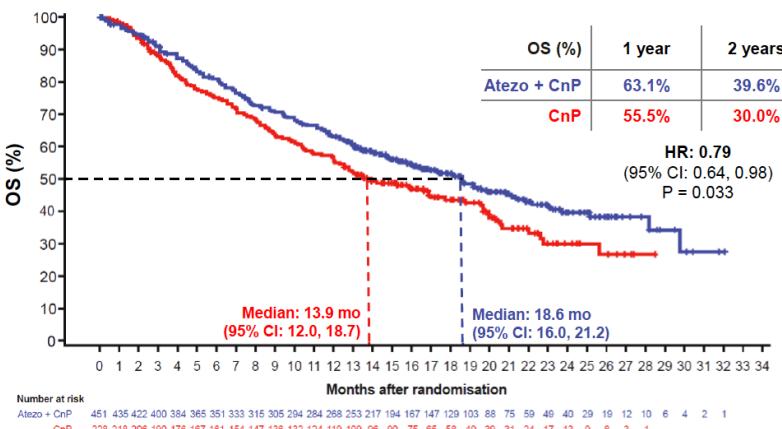
Investigator-assessed PFS (ITT-WT)

MUNICH ESMO congress 2018

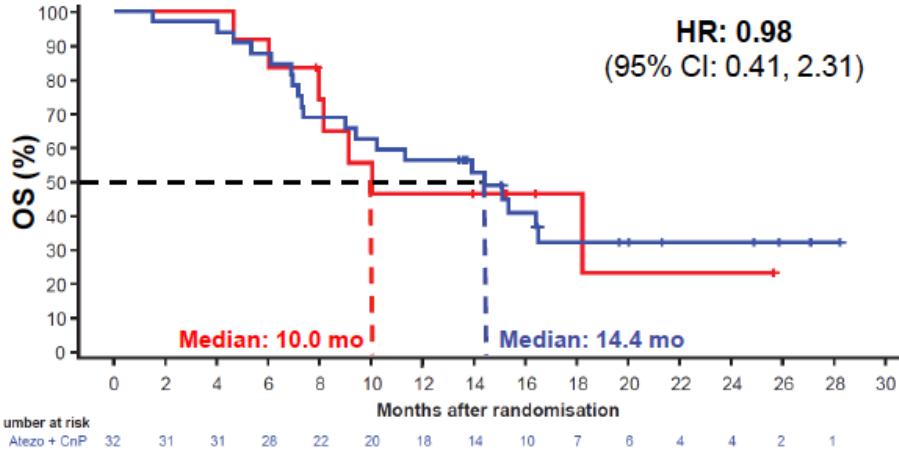


OS (ITT-WT)

MUNICH ESMO congress 2018

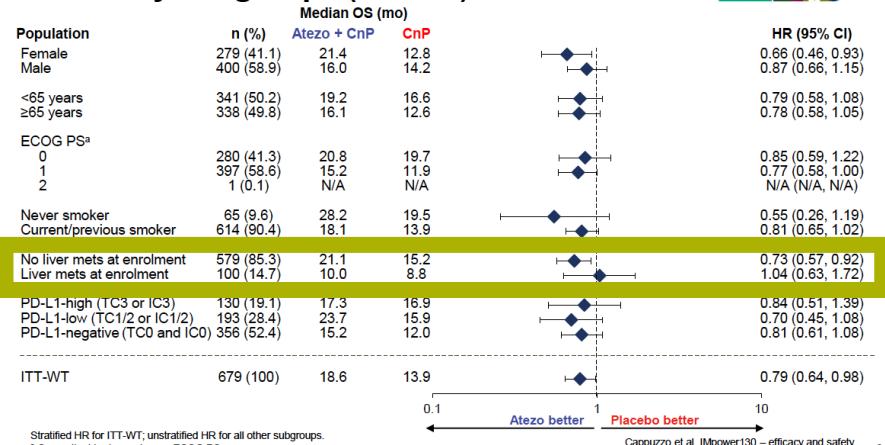


IMPower130: special populations



OS in EGFR/ALK NSCLC

OS in key subgroups (ITT-WT)

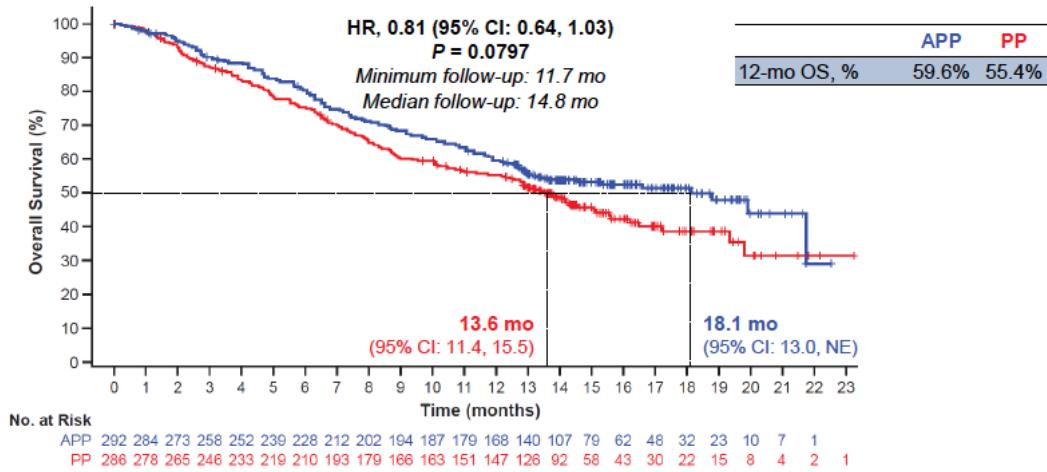
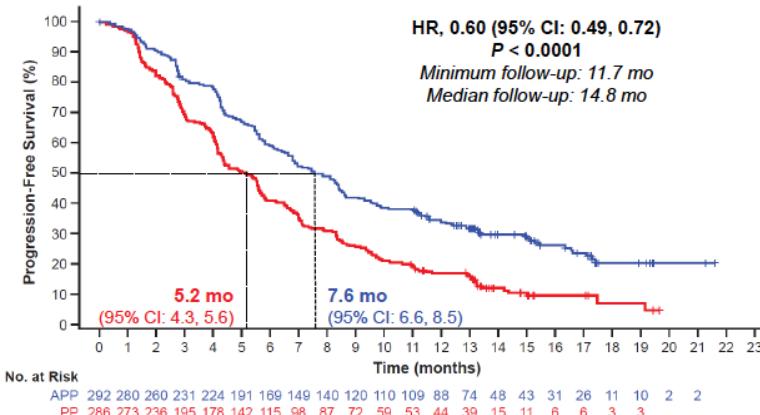


Role of angiogenesis in liver

IMPower132: non Squamous atezo + platinum/pemetrexed

- RR 47% vs 32%
- mPFS 7.6 vs 5.2 mo;
HR 0.60; p<0.0001
- mOS 18.1 vs 13.6 mo;
HR 0.81; p 0.079
(1yOS 34% vs 17%)

PFS in the ITT population¹

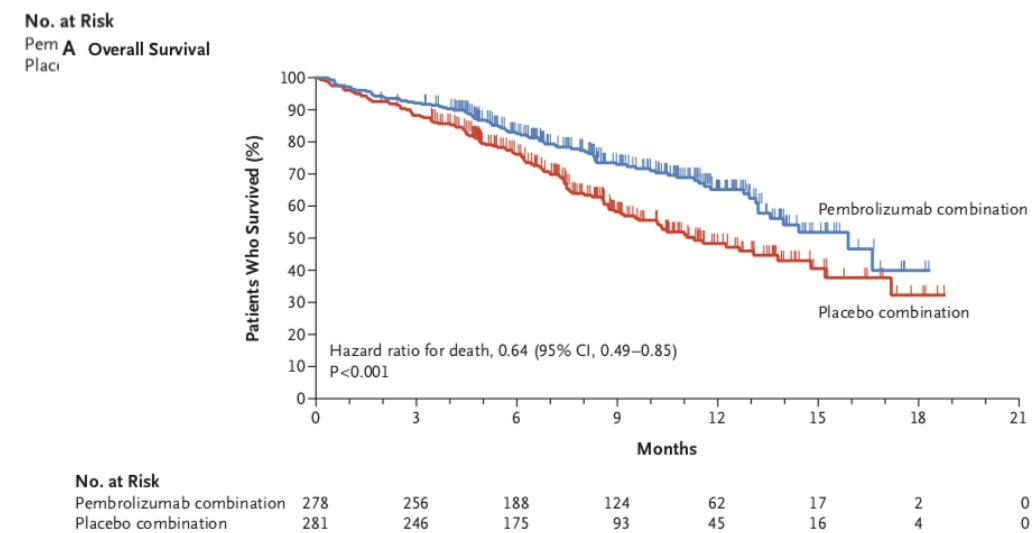
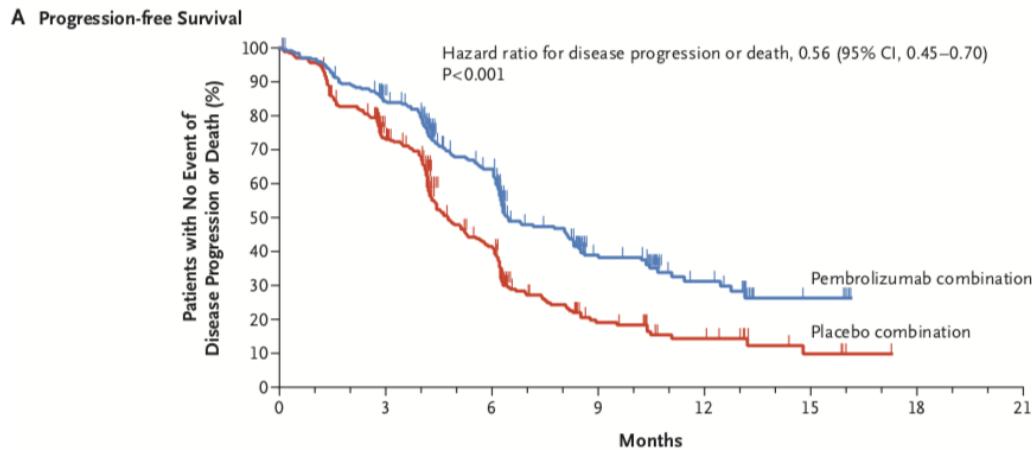


„ IO-Chemotherapy combinations in Squamous NSCLC

- Keynote-407: pembrolizumab + carboplatinum/paclitaxel or nabpaclitaxel
- IM Power 131: atezolizumab + carboplatinum + nabpaclitaxel

KEYNOTE-407: Squamous Pembrolizumab + carbo/nabpaclitaxel

- RR 58 vs 35%; $p=0.0004$
- mPFS 6.4 vs 4.8 mo;
HR 0.56; $p<0.001$
- mOS 15.9 vs 11.3 mo,
HR 0.64, $p=0.0008$

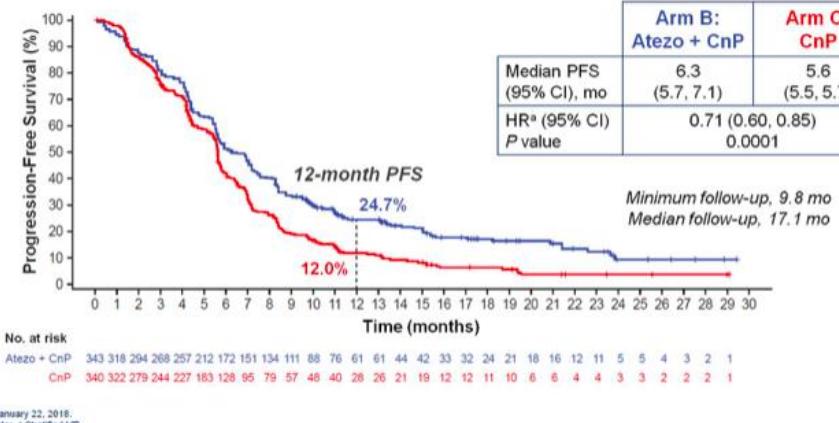


No. at Risk	278	256	188	124	62	17	2	0
Pembrolizumab combination	278	256	188	124	62	17	2	0
Placebo combination	281	246	175	93	45	16	4	0

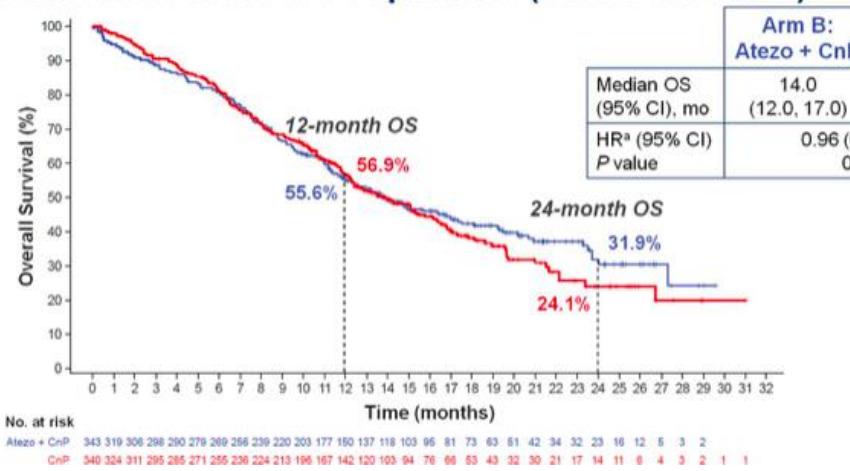
IMPower131: Squamous Atezo + carboplatin/nabpaclitaxel

- RR 49 vs 41%
- mPFS 6.3 vs 5.6 mo;
HR 0.71; p=0.0001
- Interim OS 14 vs 13.9 mo;
HR 0.96; p=0.69

INV-Assessed PFS in the ITT Population (Arm B vs Arm C)



First Interim OS in the ITT Population (Arm B vs Arm C)

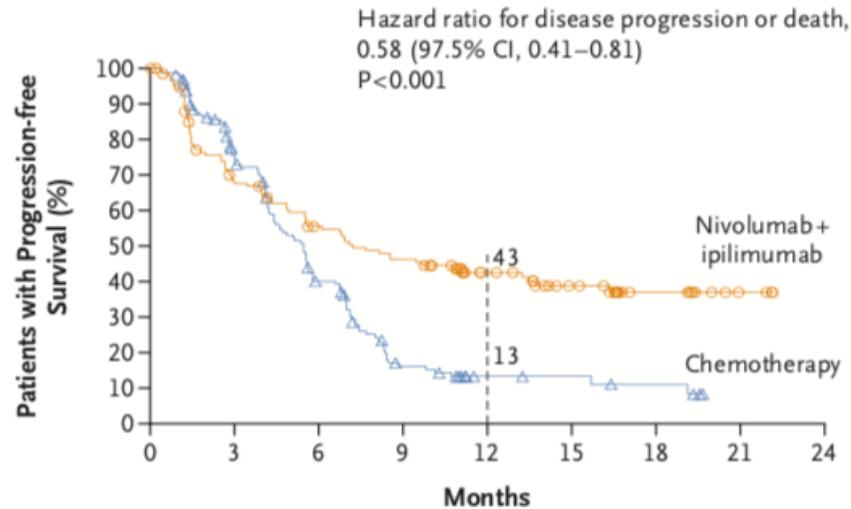


IO-IO combination Checkmate 227: Nivolumab/Ipilimumab

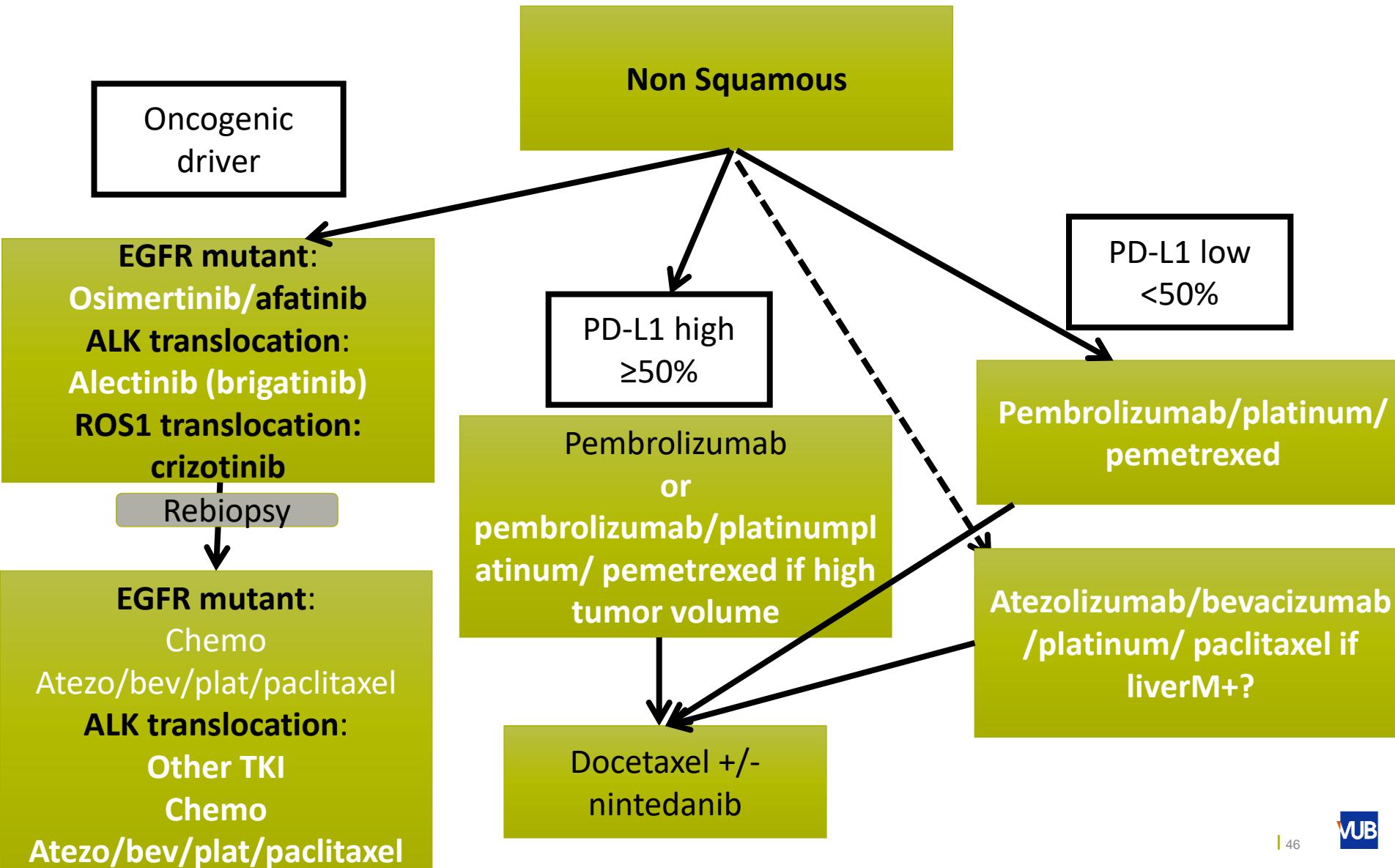
- RR 45.3 vs 26.9%
- mPFS 7.2 vs 5.5 mo;
HR 0.58; p<0.001
1yPFS 42.6 vs 13.2%
- mOS 23 mo vs 16.7 mo;
HR 0.77
- In low TMB <10 mut/Mb
➤ mOS 16.2 vs 12.4 mo HR 0.78

Nivo 3 mg/kg q2w + Ipi 1 mg/kg q6w
High TMB \geq 10 mutations per Mb

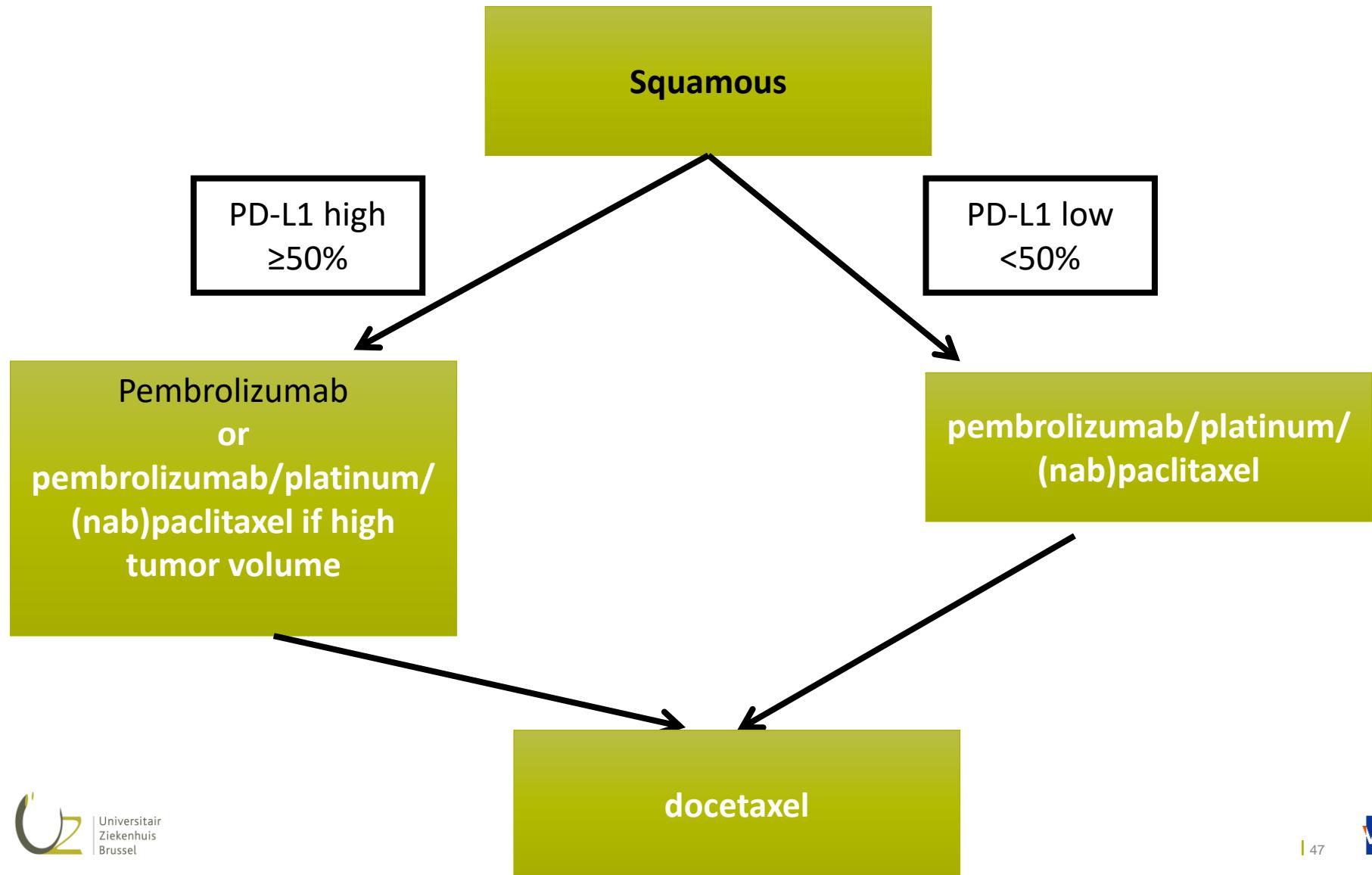
A Progression-free Survival



NSCLC 2019



NSCLC 2019



☰ Overview

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2. Metastatic NSCLC

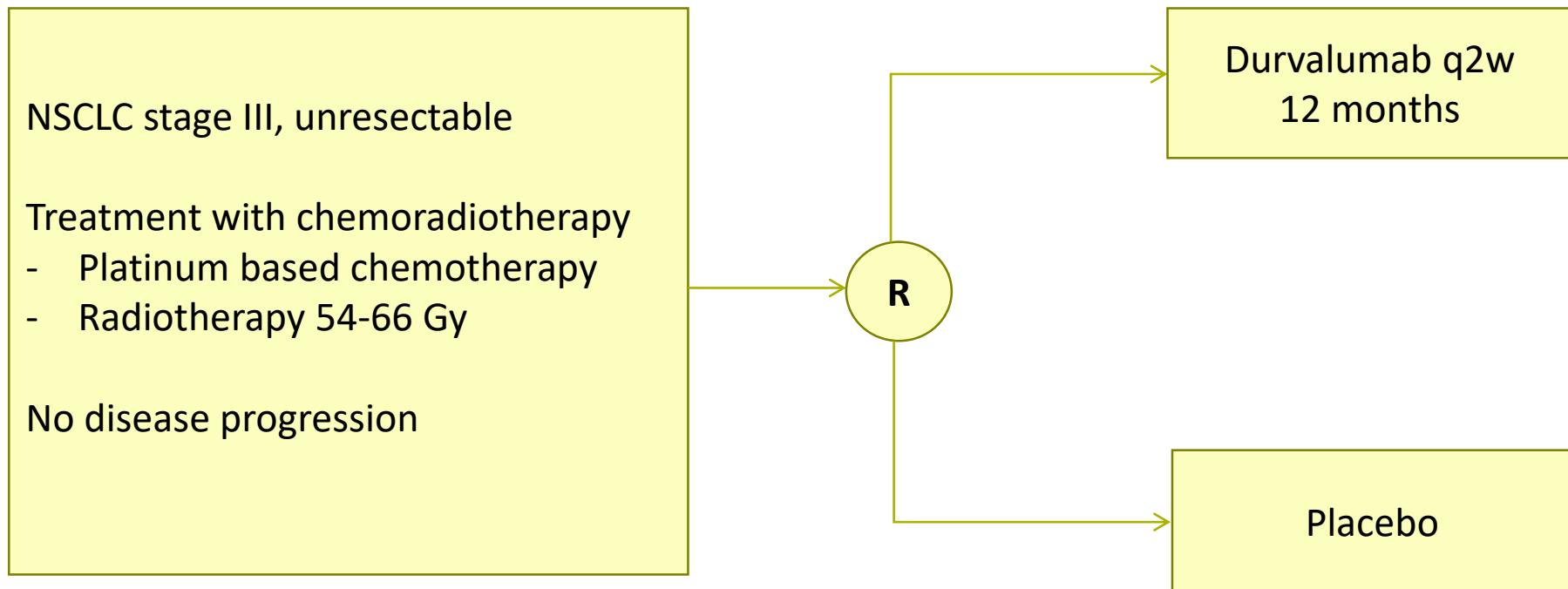
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PACIFIC: NSCLC stage III after chemoradiotherapy

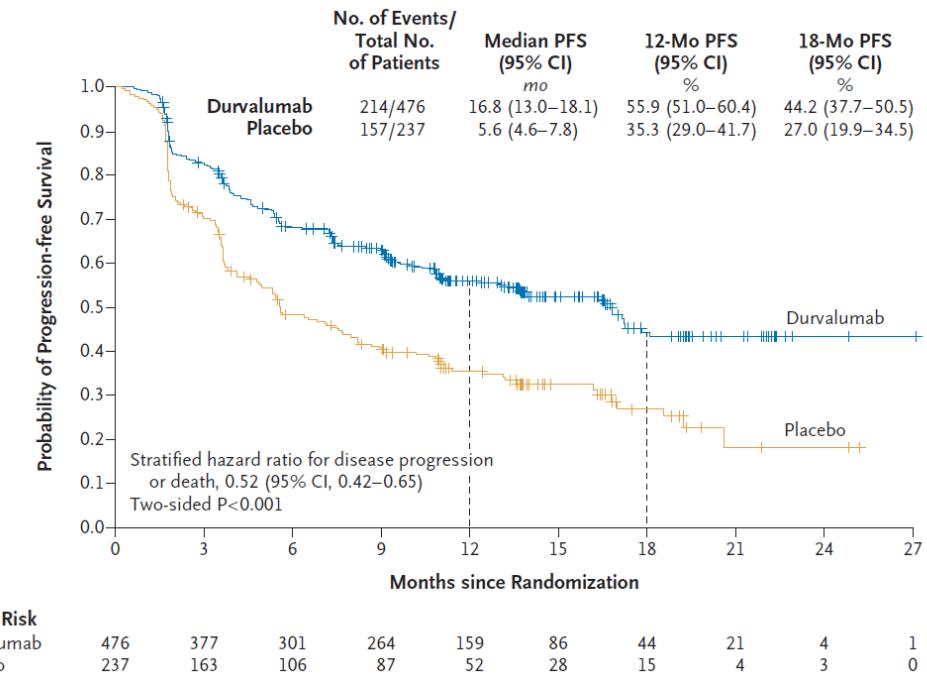
Phase III study with Durvalumab (PACIFIC), unselected!



PACIFIC

Durvalumab after ccRTCT

- mPFS 16.8 vs 5.6 mo;
HR0.52; p<0.0001
- 1yPFS 55.9 vs 35.3%

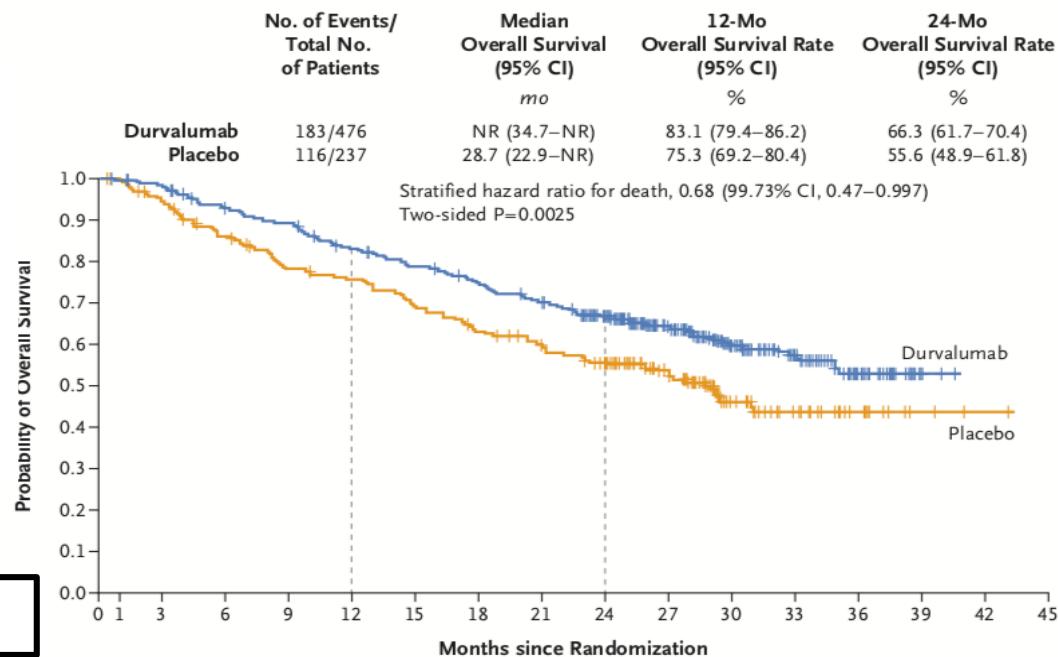


Antonia SJ et al. N Eng J Med 2017

PACIFIC

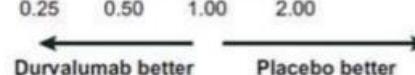
Durvalumab after ccRTCT

- mOS NR vs 28,7 m;
HR 0.68; p=0.0025
- 1y OS 83 vs 75%



BUT: NO OS benefit in PD-L1<1%

Subgroup	Durvalumab no. of events / no. of patients (%)	Placebo no. of events / no. of patients (%)	Unstratified Hazard Ratio for Death (95% CI)
All patients	183/476 (38.4)	116/237 (48.9)	0.68 (0.53–0.87) ^c
PD-L1 status			
≥1%	70/212 (33.0)	45/91 (49.5)	0.53 (0.36–0.77)
≥25%*	37/115 (32.2)	23/44 (52.3)	0.46 (0.27–0.78)
1–24%	33/97 (34.0)	22/47 (46.8)	0.60 (0.35–1.03)
<1%	41/90 (45.6)	19/58 (32.8)	1.36 (0.79–2.34)
Unknown	72/174 (41.4)	52/88 (59.1)	0.62 (0.43–0.89)



☰ Overview

1. Introduction

2. Metastatic NSCLC

- Metastatic NSCLC before 2018
- Novelties in targeted therapies
- Novelties in immunotherapy

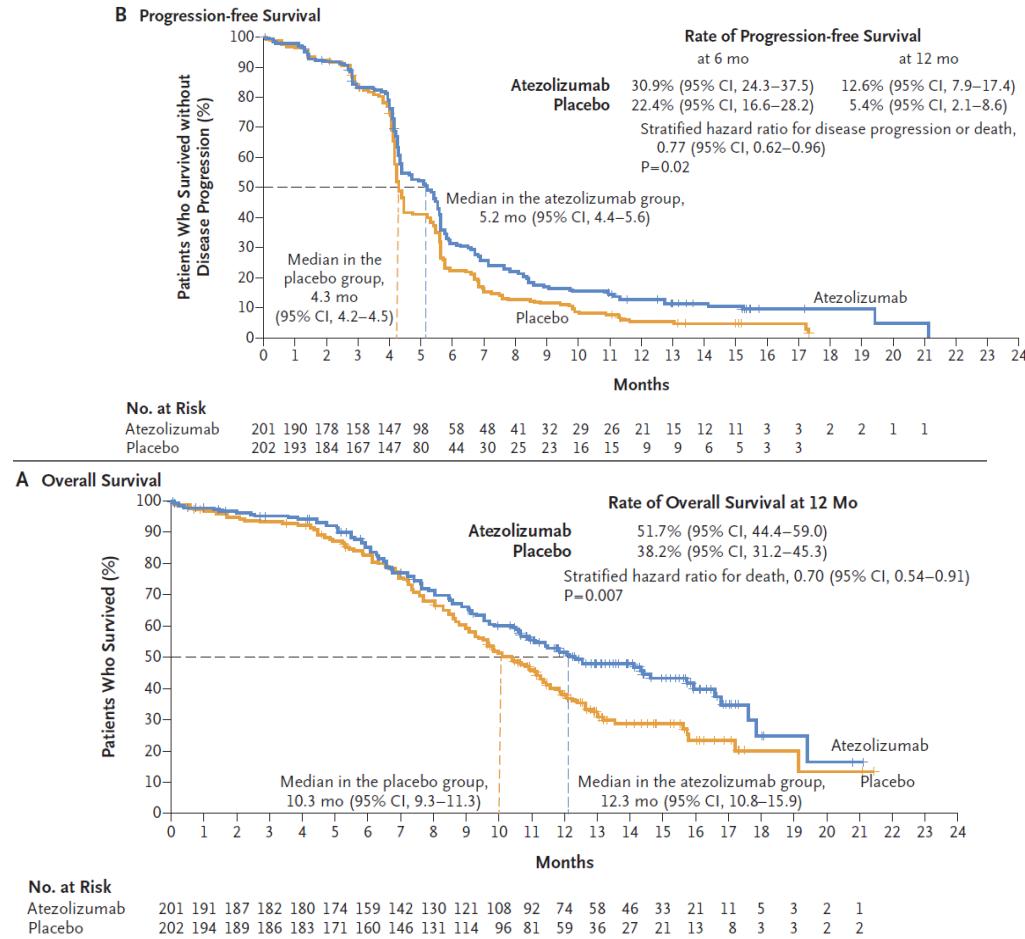
3. Locally advanced NSCLC

4. Immunotherapy in advanced SCLC

III Advanced small cell lung cancer

➤ Carboplatinum/etoposide + atezolizumab/placebo

- mPFS 5.2 vs 4.3 mo;
HR 0.77; p=0.02
- 1y PFS 12.6% vs 5.4%
- mOS 12.3 vs 10.3 mo;
HR 0.70; p=0.07
- 1y OS 51.7 vs 38.2%



III Conclusions

- New generation TKIs are becoming standard of care in first line NSCLC with an oncogenic driver
- IO has changed the landscape of NSCLC without an oncogenic driver and of SCLC
- Need to identify those patients that benefit the most!!

" Future ...

