

**14th BSMO Bordet Symposium on the Integration of Molecular Biology  
Advances into Oncology Clinical Practice**

# **Biologicals and CPIs in NSCLC : the state of the art in 2020**

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Head of the EORTC Lung Cancer Group

# Disclosures

- **No personal financial disclosures**
- **Sponsored Research at Gustave Roussy Cancer Center**  
Abbvie, Amgen, AstraZeneca, BeiGene, Blueprint Medicines, BMS, Boehringer Ingelheim, Celgene, Cristal Therapeutics, Daiichi-Sankyo, Eli Lilly, GSK, Ignyta, IPSEN, Inivata, Janssen, Merck KGaA, MSD, Nektar, Onxeo, OSE immunotherapeutics, Pfizer, Pharma Mar, Roche-Genentech, Sanofi, Servier, Spectrum Pharmaceuticals, Takeda, Tiziana Pharma, Tolero Pharmaceuticals.
- **Investigator or co-investigator of trials**  
Nerviano, GSK, Pfizer, Roche-Genentech, Lilly, OSE Pharma, MSD, Celgene, Stemcentrx, Ignyta, Abbvie, Loxo Oncology, AstraZeneca, Blueprint Medicines.

# New treatment paradigm in NSCLC

Oncogene addiction

PD-L1

EGFR

ALK

ROS1

BRAF  
V600E

NTRK

PD-L1< 1%

PD-L1 1-49%

PD-L1 $\geq$  50%

**Targeted therapies**

**Immunotherapy**

**Chemotherapy + Immunotherapy**

**Immunotherapy + Immunotherapy**

**Today, you need : EGFR, BRAF mut (+KRAS)  
IHC (FISH) ALK/ROS1/NTRK  
IHC PD-L1**

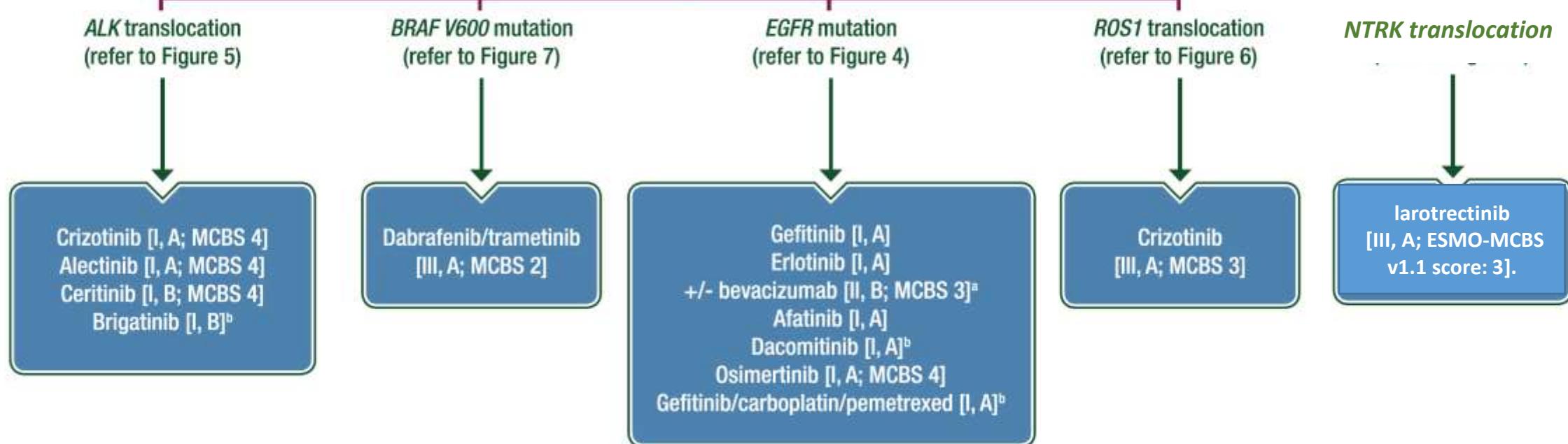
**Never smokers+++**

Algorithm by Jordi Remon

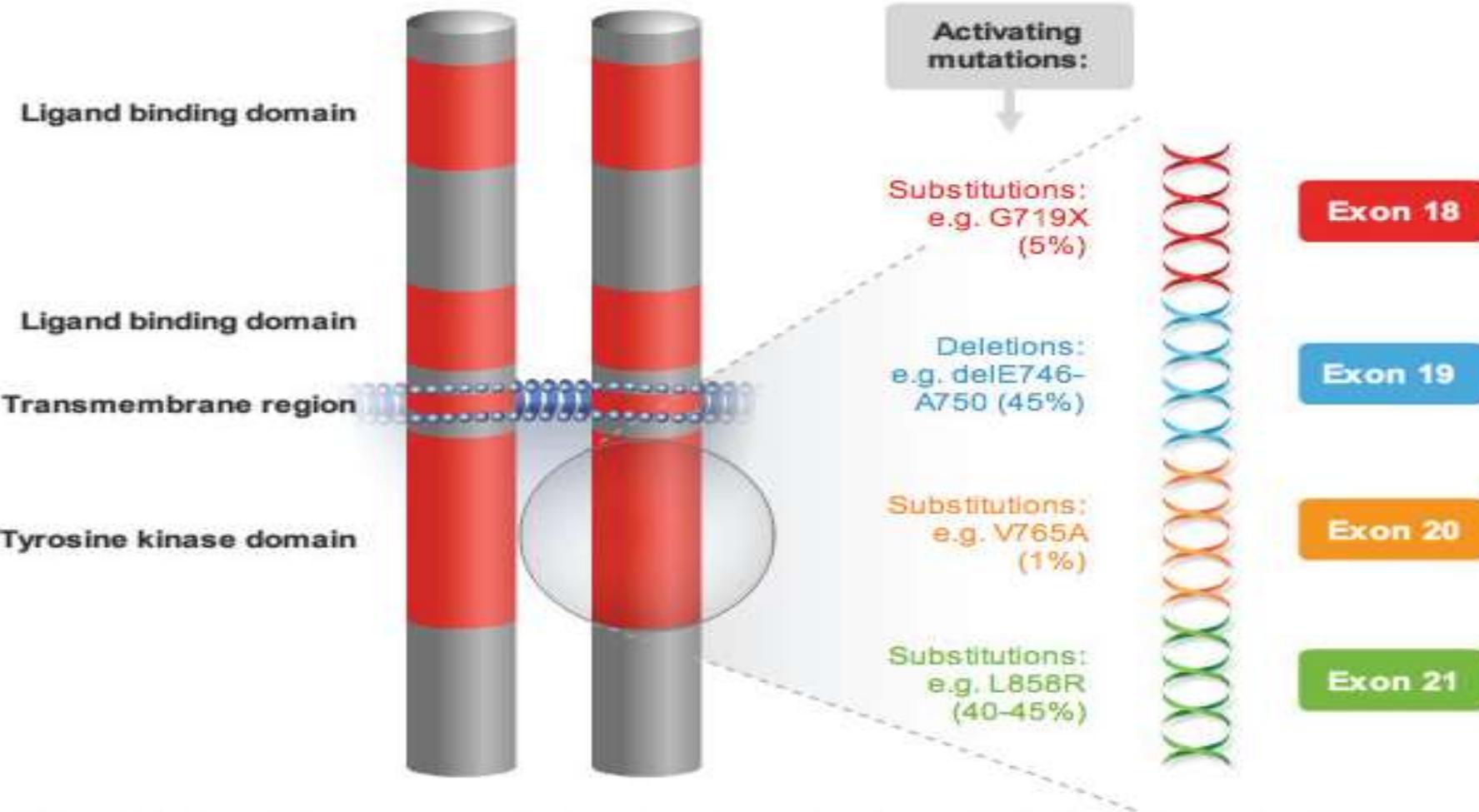
Modified from Jordi Remon

# ESMO Clinical Practice Guidelines

## Stage IV NSCC: Molecular tests positive (*ALK/BRAF/EGFR/ROS1*)



# EGFR mutations in lung cancer

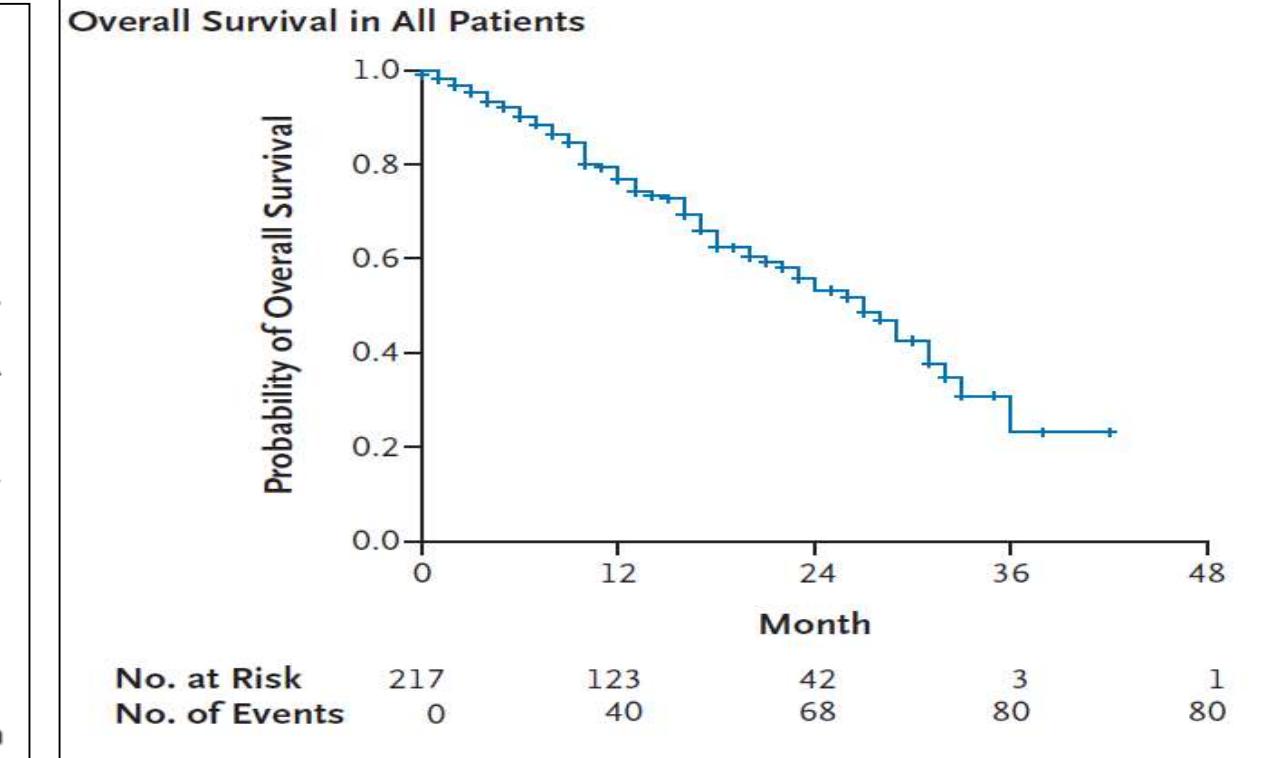
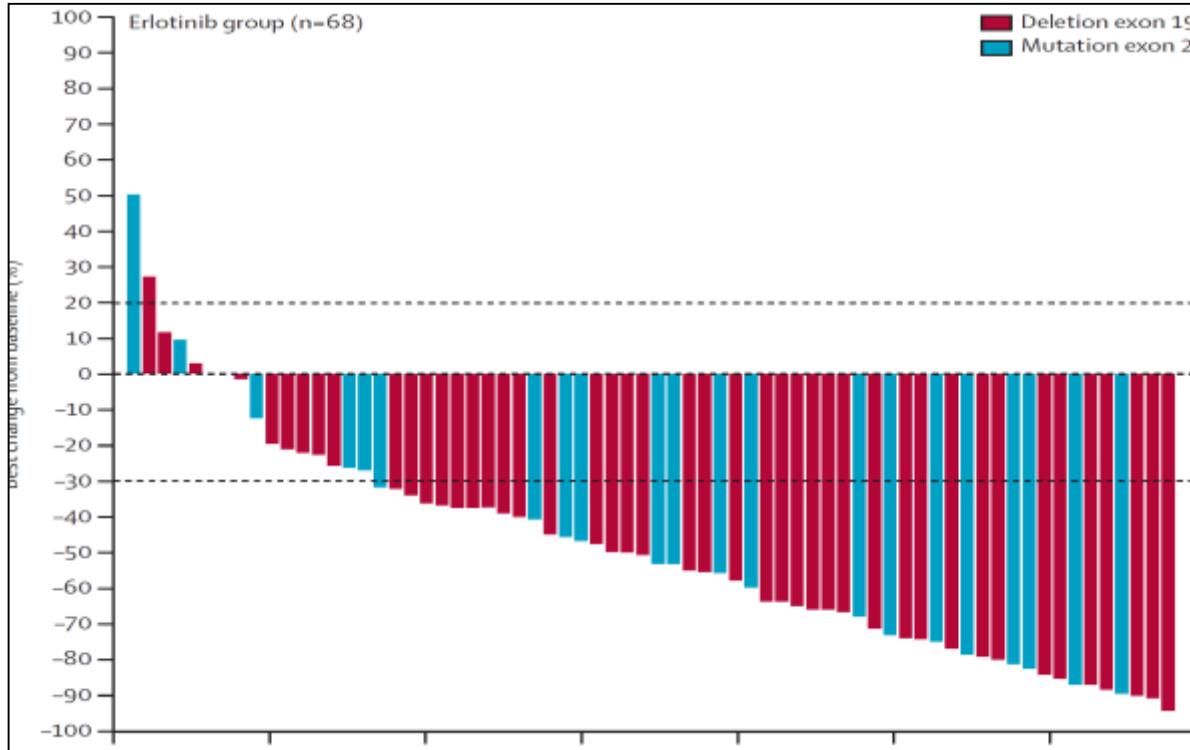


**ACTIVATING  
MUTATIONS**

**mostly  
exon 19 del  
&  
exon 21 L858R**

\* T790M <5% at initial EGFR mutations, however it is the major resistance mutation (50%) after treatment with reversible TKIs

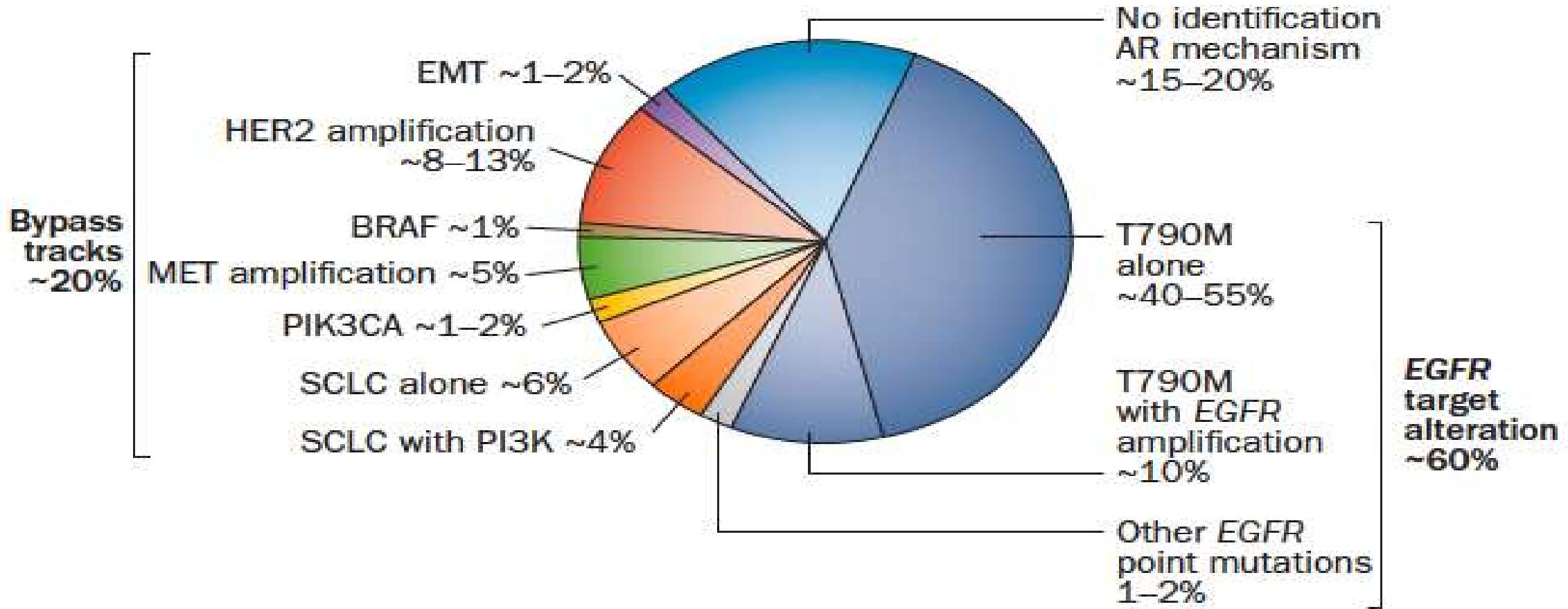
# EGFR inhibitor in EGFR mut NSCLC



Response rate : 58%

Median OS: 27 months

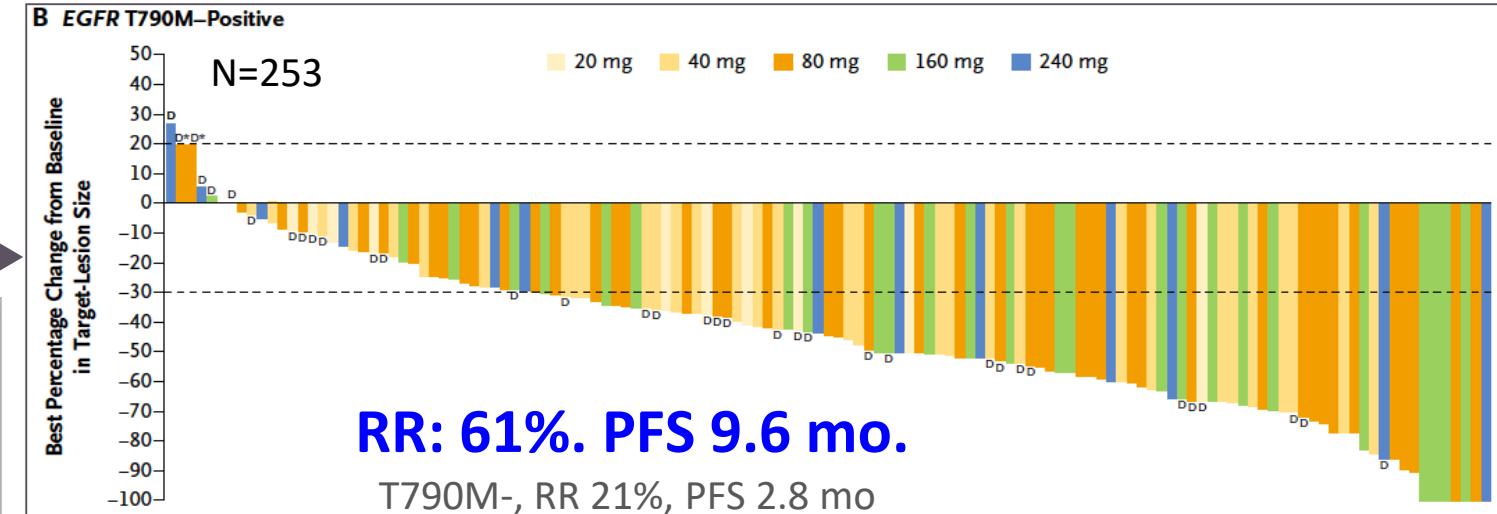
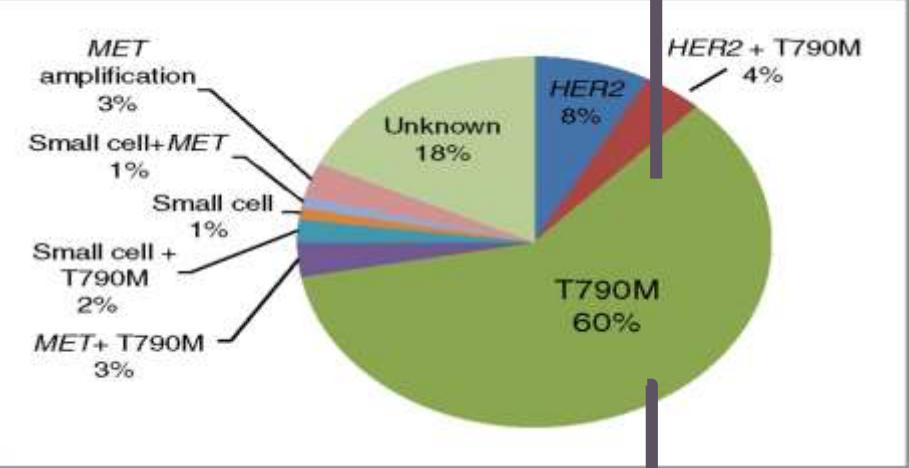
# Acquired resistance to EGFR TKI



# Acquired resistant to EGFR TKI. T790M

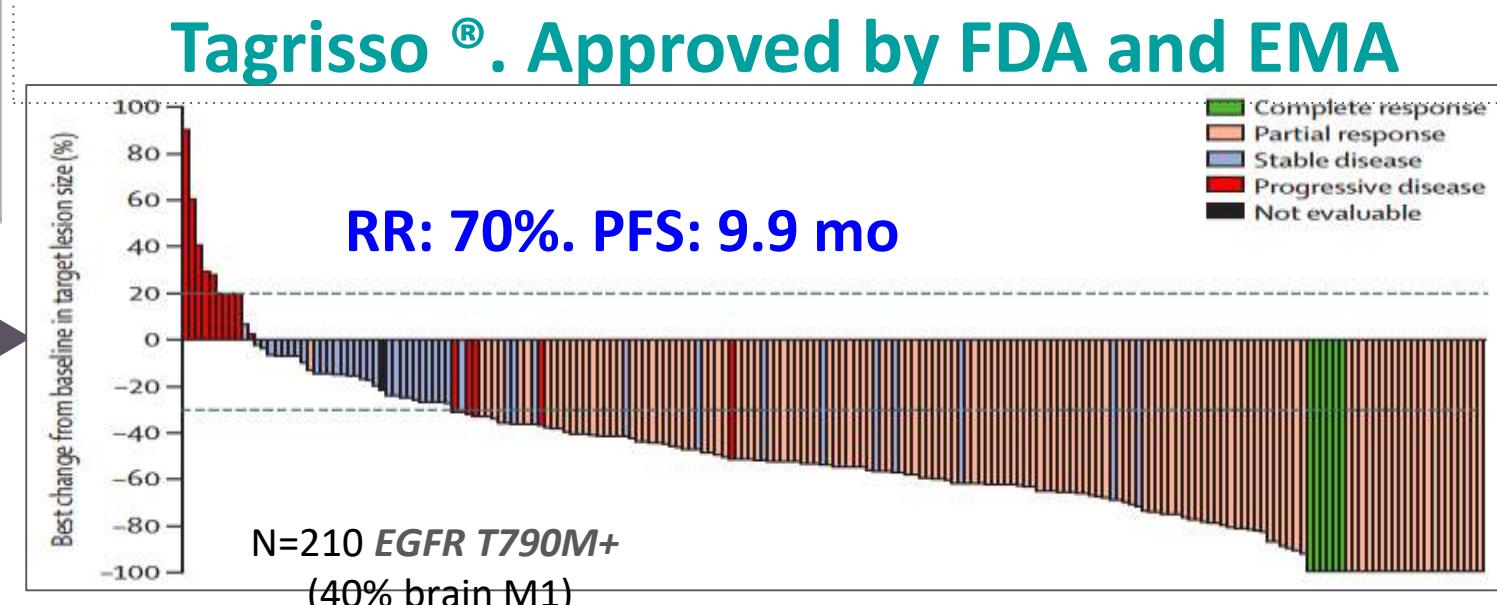
## 3<sup>rd</sup> GENERATION

### Osimertinib, Phase I

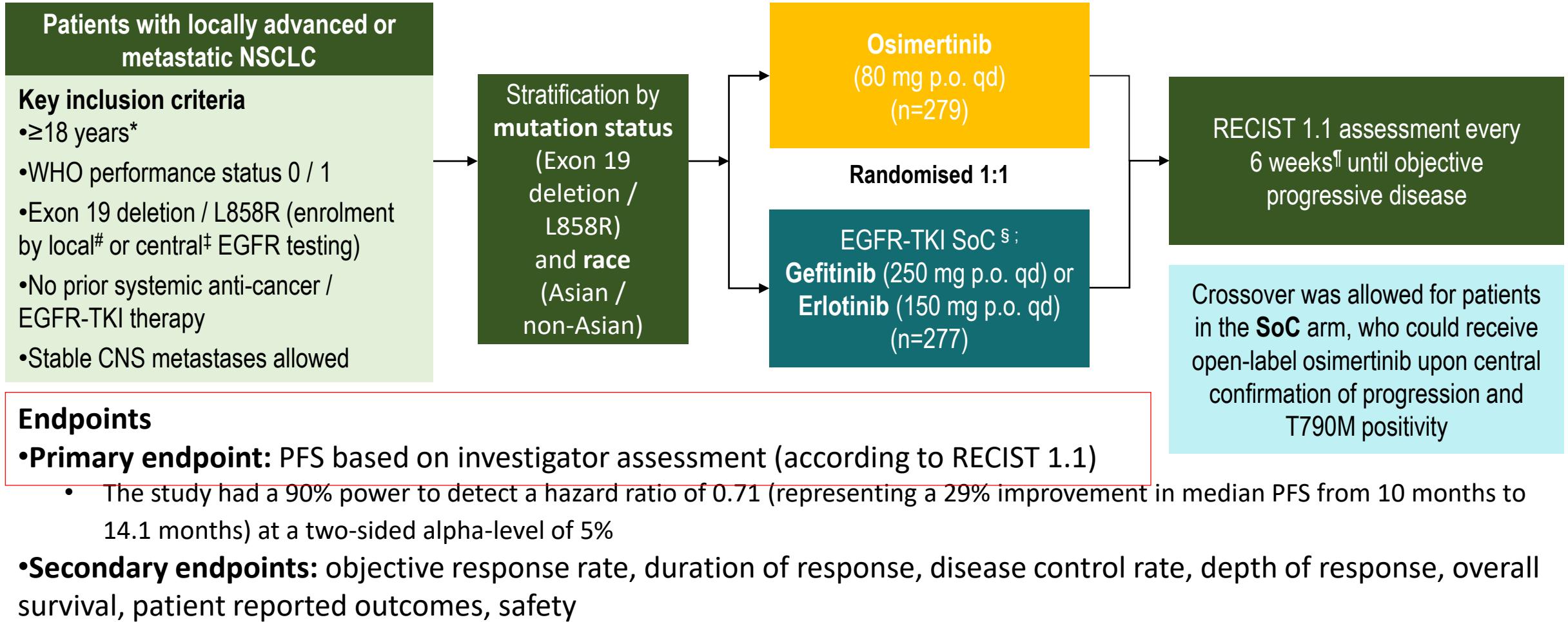


### Osimertinib, Phase II

AURA3 (T790M+), ph3: AZD9291 > CT



# FLAURA Trial: Osimertinib vs. SOC



## Endpoints

**Primary endpoint:** PFS based on investigator assessment (according to RECIST 1.1)

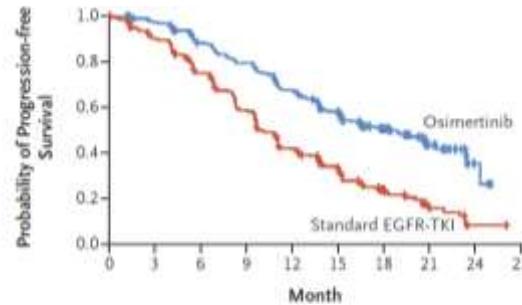
- The study had a 90% power to detect a hazard ratio of 0.71 (representing a 29% improvement in median PFS from 10 months to 14.1 months) at a two-sided alpha-level of 5%

**Secondary endpoints:** objective response rate, duration of response, disease control rate, depth of response, overall survival, patient reported outcomes, safety

~20% brain mets at baseline

# FLAURA trial: PFS and OS

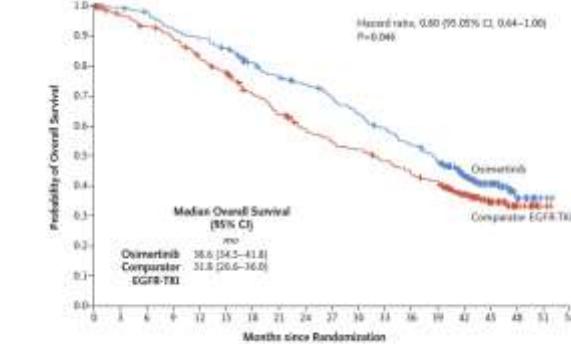
PFS



No. at Risk	Osimertinib	Standard EGFR-TKI
279	277	
262	239	
233	197	
210	152	
178	107	
139	78	
71	37	
26	10	
4	2	
0	0	

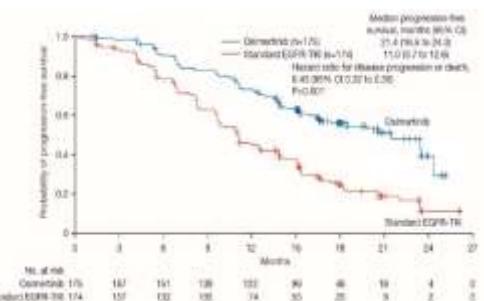
**18.9 vs 10.2 mo**  
**HR 0.46 (95% CI 0.37-0.57)**

OS



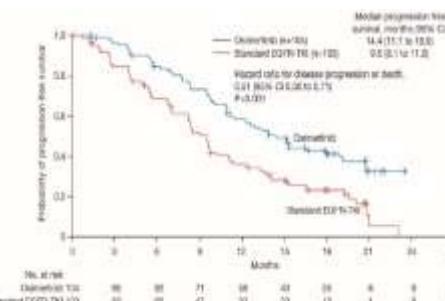
**38.6 vs 31.8 mo**  
**HR 0.80 (95% CI 0.64-1.00)**

Exon 19



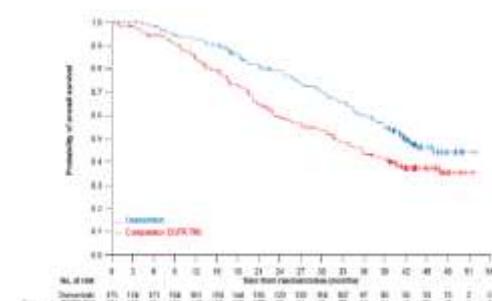
**21.4 vs 11.0 mo**  
**HR 0.43 (95% CI 0.32-0.56)**

Exon 21



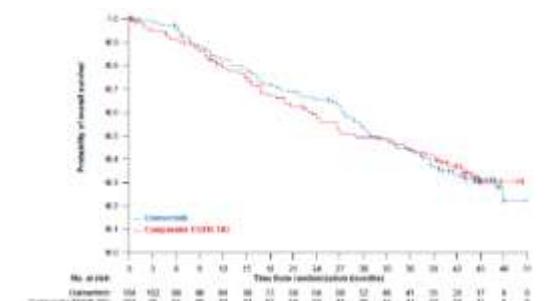
**14.4 vs 9.5 mo**  
**HR 0.51 (95% CI 0.36-0.71)**

Exon 19



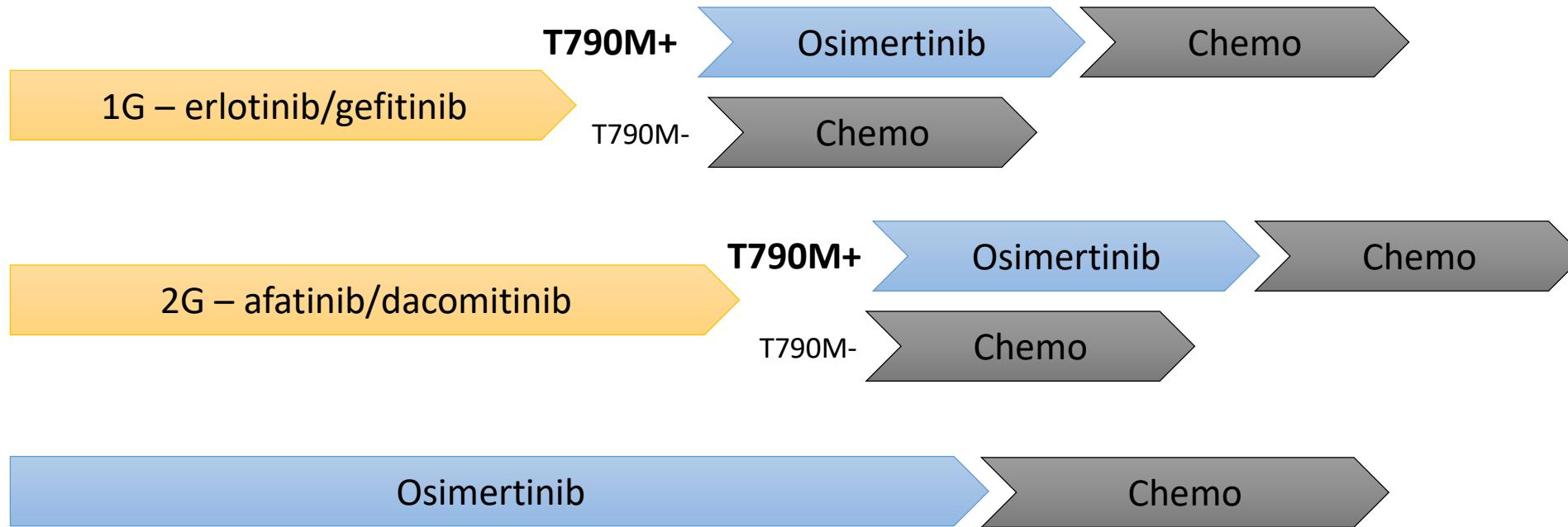
**HR 0.68 (95% CI 0.51-0.90)**

Exon 21

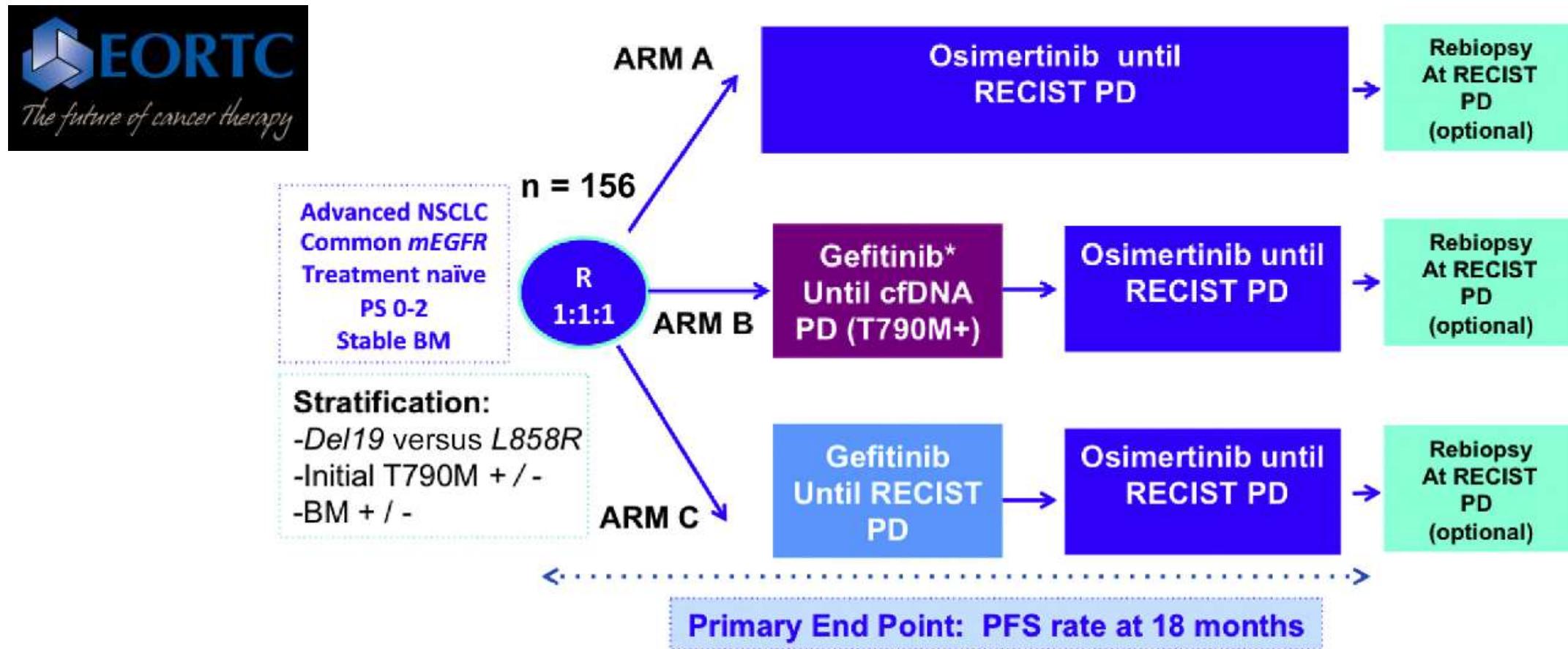


**HR 1.00 (95% CI 0.71-1.40)**

# Treatment strategies



# APPLE study: relevance of “molecular” PD



(cfDNA using cobas every 4 weeks and CT scan of the brain-thorax-abdomen every 8 weeks all arms)

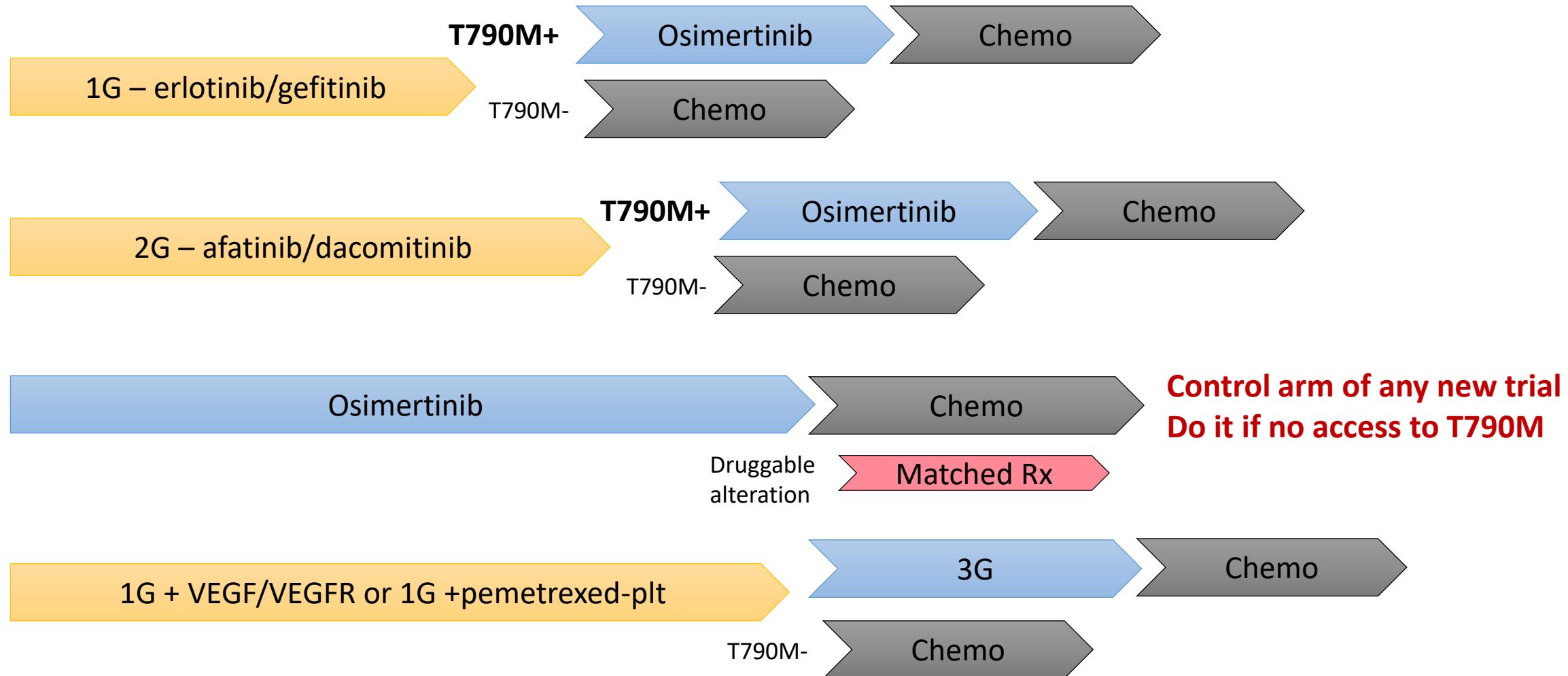
\*In case of RECIST progression without T790M+, patients will be switched

Trial	TKI	Comparing Tx	ORR %	PFS (months)	HR	OS (months)
iPASS	Gefitinib	Cb/Pac	71 v 47	9.5 v 6.3	0.48 (0.36-0.64)	21.6 v 21.9 (NS)
First-Signal	Gefitinib	Cis/Gem	55 v 46	8.0 v 6.4	0.54 (0.26-1.10)	27.2 v 25.6 (NS)
WJTOG	Gefitinib	Cis/Doc	62 v 32	9.2 v 6.3	0.49 (0.34-0.71)	34.9 v 37.3 (NS)
NEJ002	Gefitinib	Cb/Pac	74 v 31	10.8 v 5.4	0.35 (0.22-0.41)	30.5 v 23.6 (NS)
OPTIMAL	Erlotinib	Cis/Gem	83 v 36	13.1 v 4.6	0.16 (0.10-0.26)	22.8 v 27.2 (NS)
EURTAC	Erlotinib	Cis/Doc or Gem	58 v 15	10.4 v 5.1	0.34 (0.23-0.29)	19.3 v 19.5 (NS)
LUX-Lung 3	Afatinib	Cis/Pem	62 v 22	13.6 v 6.9	0.47 (0.34-0.65)	31.6 v 28.2 (NS)
LUX-Lung 6	Afatinib	Cis/Gem	68 v 23	11.0 v 5.6	0.25 (0.20-0.39)	23.6 v 23.5 (NS)
LUX-Lung 7	Afatinib	Gefitinib	70 v 56	11.0 v 10.9	0.74 (0.57-0.95)	27.9 v 24.5 (NS)
ARCHER 1050	Dacomitinib	Gefitinib	75 v 72	14.7 v 9.2	0.59 (0.47-0.74)	34.1 v 26.8 (S)
FLAURA*	Osimertinib	Gefitinib/ Erlotinib	80 v 76	18.9 v 10.2	0.46 (0.37-0.57)	38.6 v 31.8 (S)
NEJ 026	Erlotinib / BVZ	Erlotinib	72 v 67	16.9 v 13.3	0.60 (0.42-0.88)	50.7 v 46.2 (NS)
ARTEMIS	Erlotinib / BV.	Erlotinib	86 v 85	18.0 v 11.3	0.55 (0.41-0.75)	Not mature
RELAY*	Erlotinib / Ramucirumab	Erlotinib	76 v 77	19.4 v 12.4	0.59 (0.46-0.76)	Not mature (NS)
CTONG 1706	Gefitinib / Apatinib	Gefitinib	77 v 74	13.7 v 10.2	0.71 (0.54-0.95)	Not mature
NEJ009	Gefitinib /CG	Gefitinib	84 v 67	20.9 v 11.2	0.49 (0.39-0.62)	52.2 v 38.8 (S)
Norohona*	Gefitinib /CG	Gefitinib	75 v 62	16.0 v 8.0	0.51 (0.39-0.66)	NR v 17.0 (S)

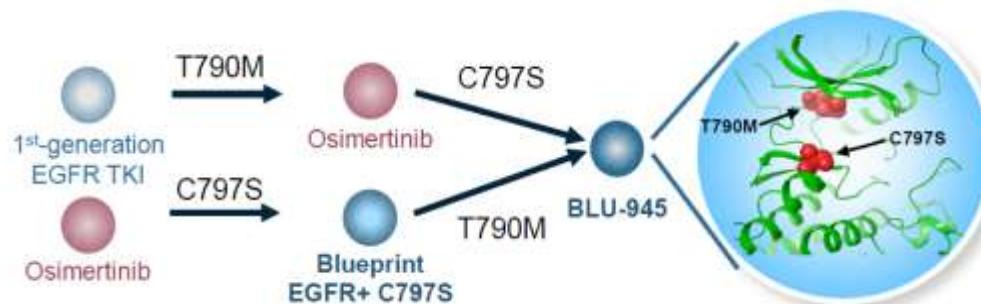
\*End point by investigator. S: significant. NS: non-significant

Courtesy of J.Remon

# Treatment strategies



# BLU-945 – Triple EGFR+/T790M/C797S

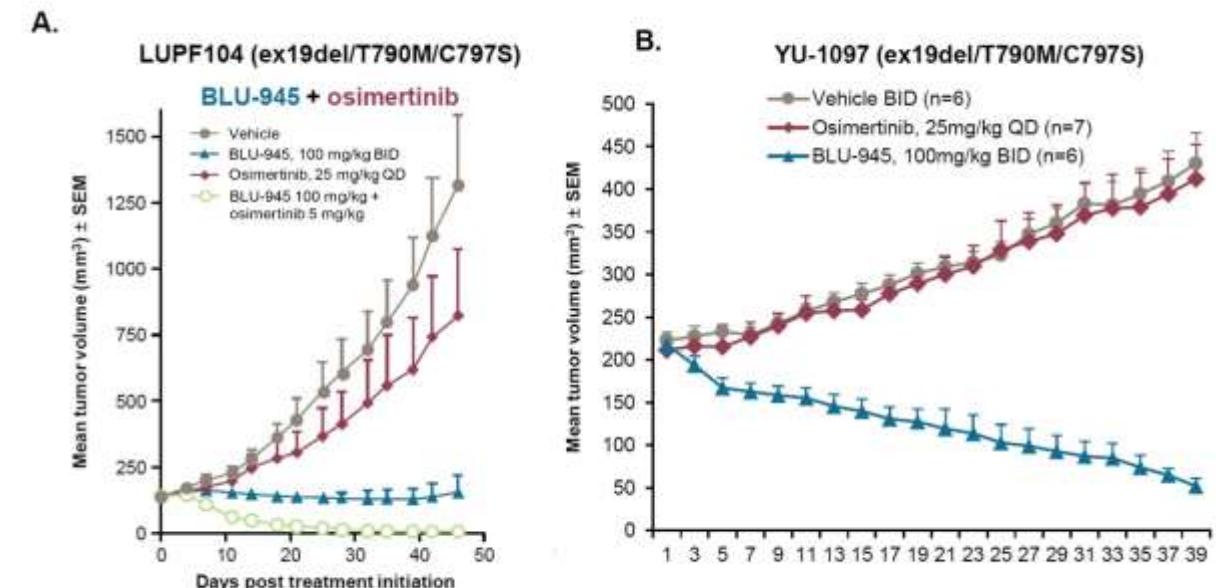


**BLU-945 inhibits EGFR+/T790M/C797S driven pathway activation**

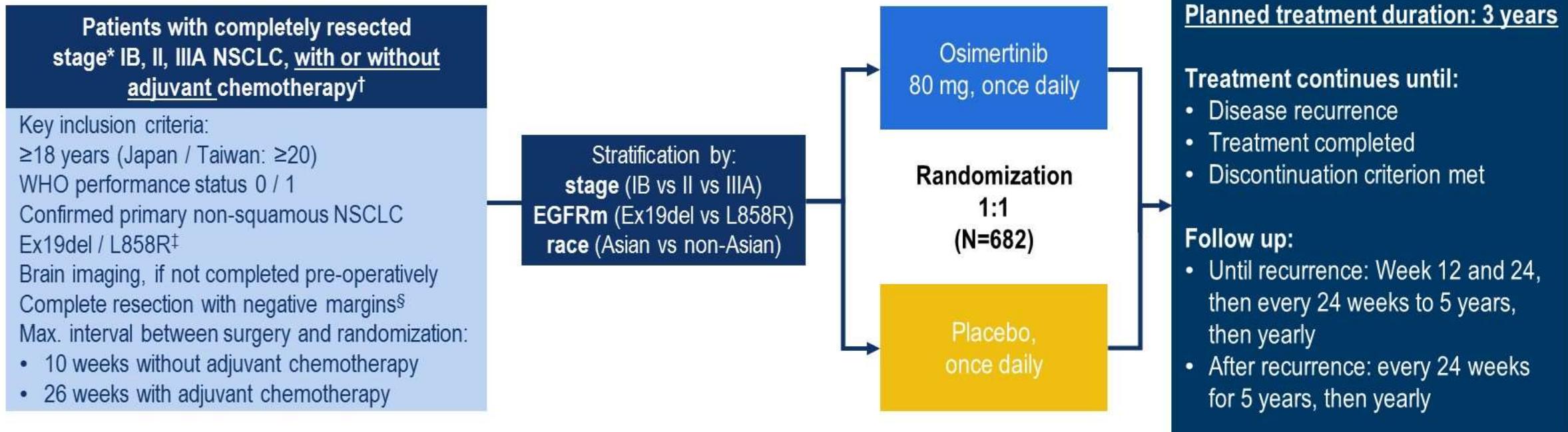
Table 2: BLU-945 potently inhibits EGFR+/T790M/C797S and EGFR+/T790M autophosphorylation

Compound	Cell lines			Engineered Ba/F3 cell lines		
	NCI-H1975 (L858R/T790M)	PC-9 (ex19del)	A431 (EGFR WT)	L858R	L858R/ T790M/C797S	ex19del/ T790M/C797S
	IC <sub>50</sub> (nM)	IC <sub>50</sub> (nM)	IC <sub>50</sub> (nM)	IC <sub>50</sub> (nM)	IC <sub>50</sub> (nM)	IC <sub>50</sub> (nM)
BLU-945	1.2	129.5	544.4	21.5	2.9	4.4
Erlotinib	>10,000	3.9	140.6	5.9	6655.5	4524.8
Gefitinib	4679.8	1.8	16.5	4.6	6707.7	4864.7
Osimertinib	4.7	2.1	115.9	11.0	7754.6	>10,000

Figure 2: BLU-945, but not osimertinib, inhibits the EGFR pathway in  
(A) ex19del/T790M/C797S and (B) L858R/T790M/C797S driven Ba/F3 cell lines



# AURA Phase III double-blind study design

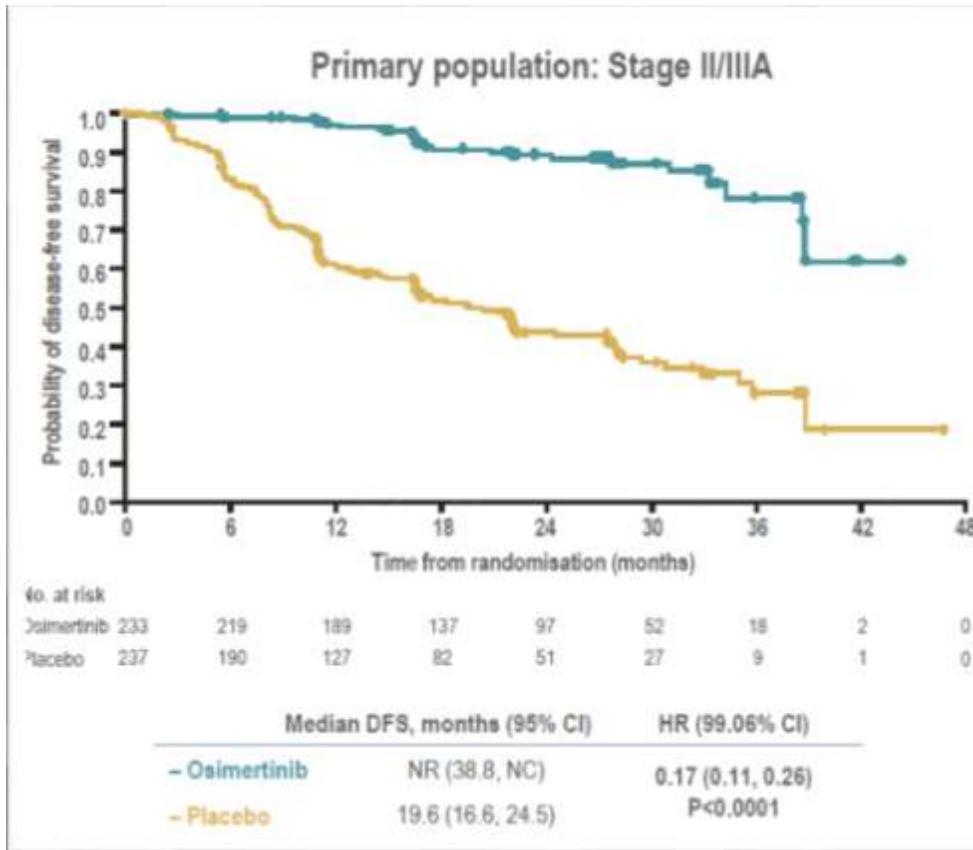


## Endpoints

- **Primary:** DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary:** DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life
- Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis
- At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year

# ADAURA

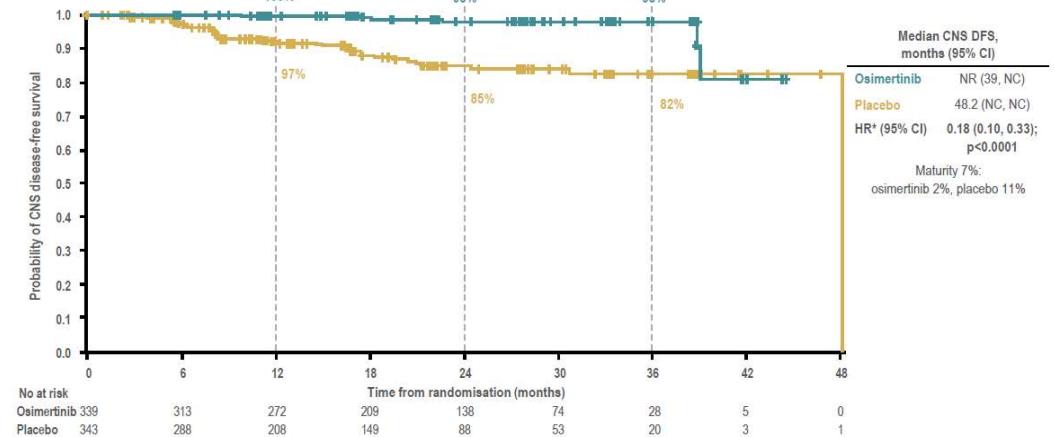
## DFS



## CNS mets

Overall population		
Patients, n (%)	Osimertinib n=339	Placebo n=343
CNS DFS events:		
CNS recurrence	6 (2%)	39 (11%)
Death <sup>†</sup>	4 (1%)	33 (10%)
	2 (1%)	6 (2%)

## CNS DFS in the overall population



Median follow-up: osimertinib 22.1 months, placebo 16.6 months;

\*A hazard ratio of <1 favours osimertinib.

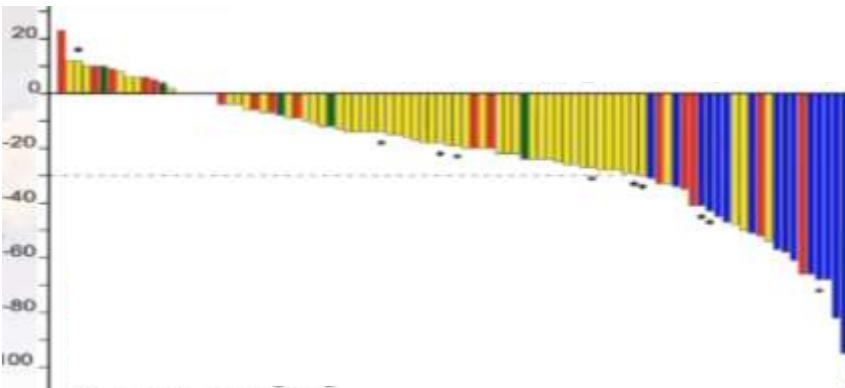
ADAURA data cut-off: 17 January, 2020

# EGFR ex20insertion, a new history begins

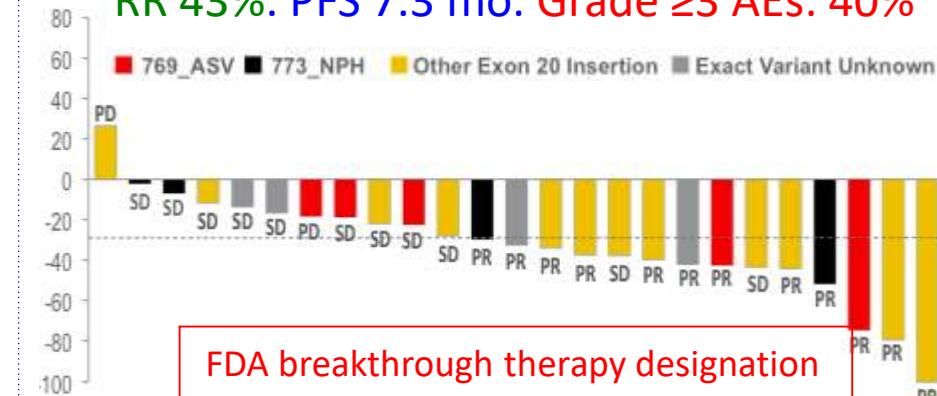
**Osimertinib 160 mg (ECOG-ACRIN 5162)**  
RR 24%. PFS 9.6 mo. Grade  $\geq 3$  AEs 29%



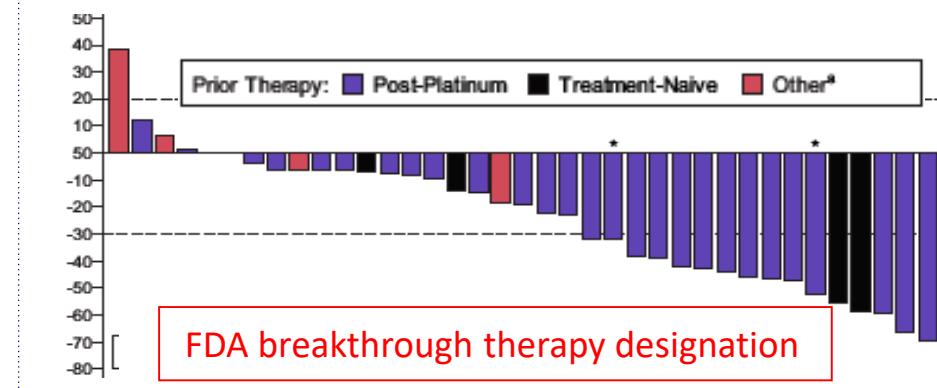
**Poziotinib (ZENNITH20)**  
RR 14.8%. PFS 4.2 mo. Grade  $\geq 3$  AEs: 60%



**Mobocertinib (TAK-788, phi/II trial)**  
RR 43%. PFS 7.3 mo. Grade  $\geq 3$  AEs: 40%

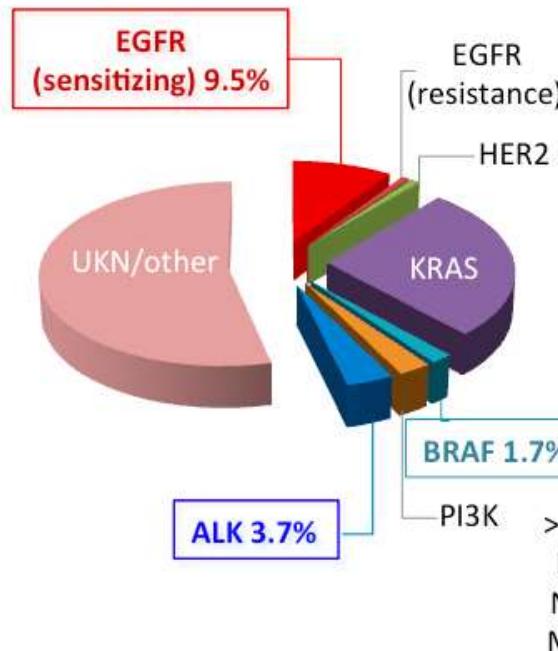


**Amivantamab (JNJ-372, CHRYSALIS)**  
RR 36%. PFS 8.3 mo. Grade  $\geq 3$  AEs: 6%

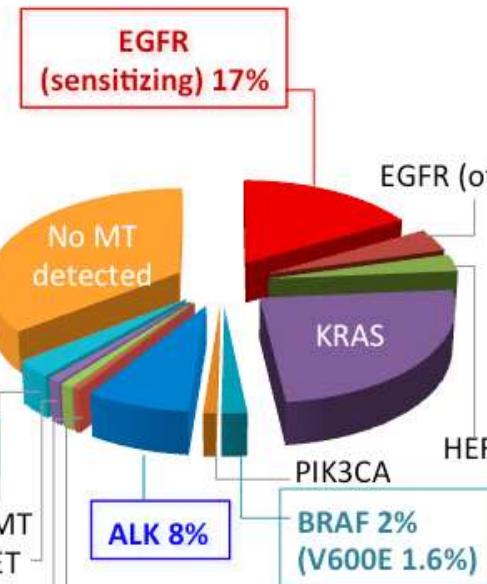


# ALK rearrangement NSCLC

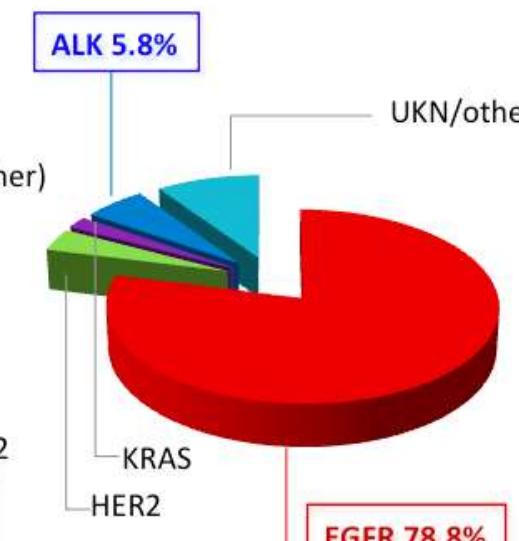
Europe (n=9,911), France<sup>1</sup>  
All histology



US (n=733), LCMC<sup>2</sup>  
Adenocarcinoma



East Asia (n=52)<sup>3</sup>  
Adenocarcinoma,  
never smokers



## FISH test



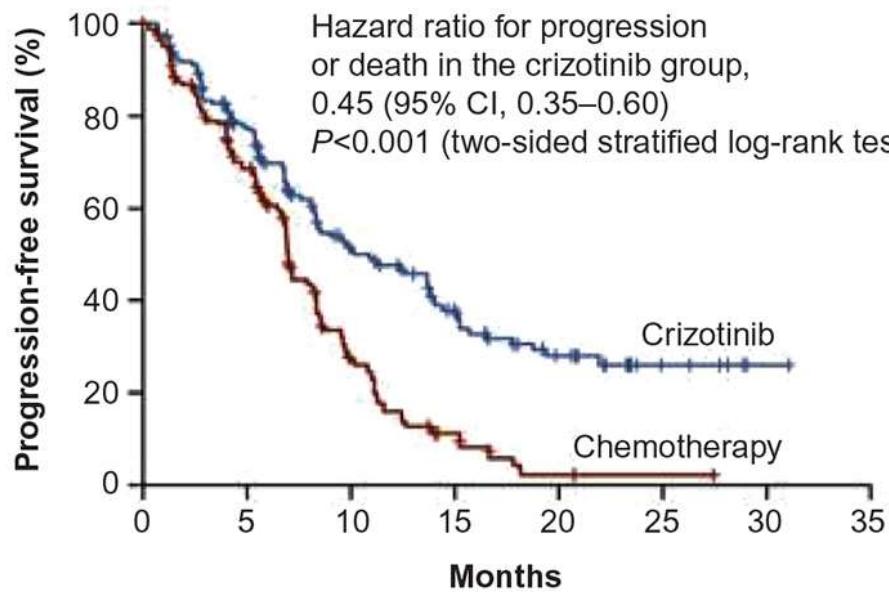
Separate red / green signals

**ALK positivity:**  
**≥15% of cells with**  
**positive pattern**

# I start with...

## Crizotinib

Progression-free survival



Number at risk

Crizotinib	172	120	65	38	19	7	1	0
Chemotherapy	171	105	36	12	2	1	0	0

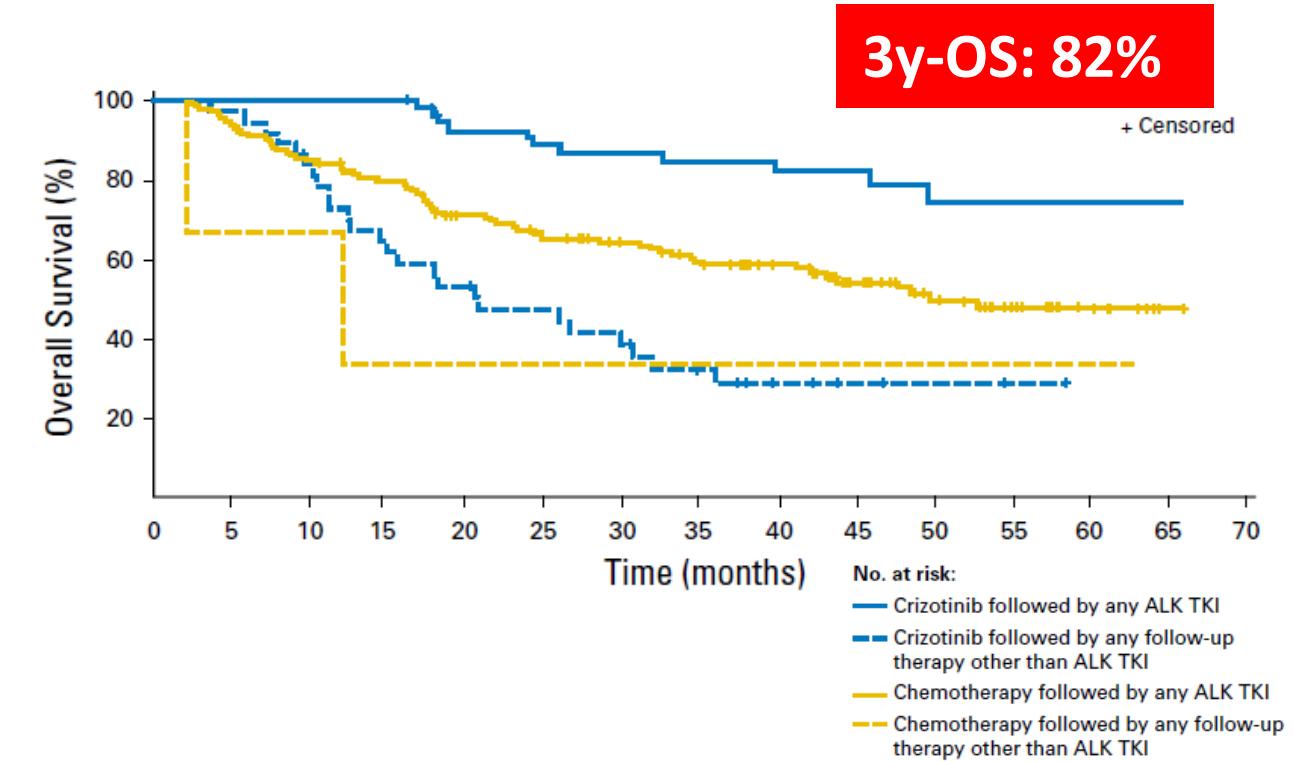
## Ceritinib

## Alectinib

## Brigatinib

## Lorlatinib

Impact of poststudy treatment on overall survival



# I start with...

Crizotinib

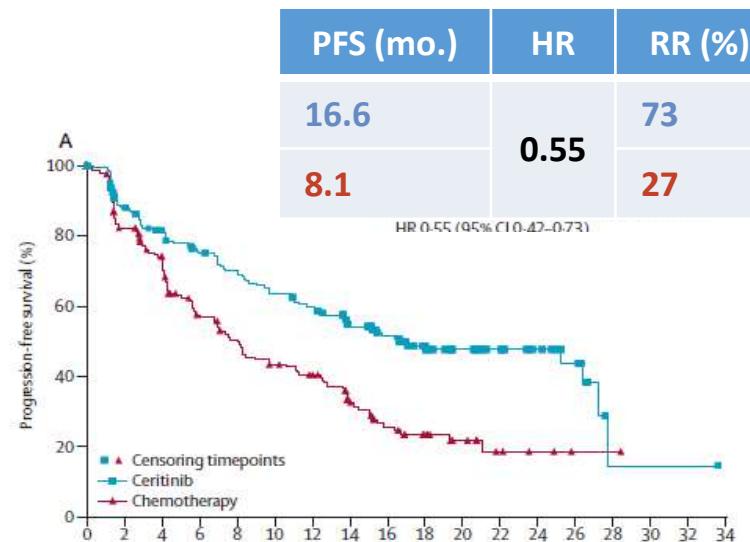
Ceritinib

Alectinib

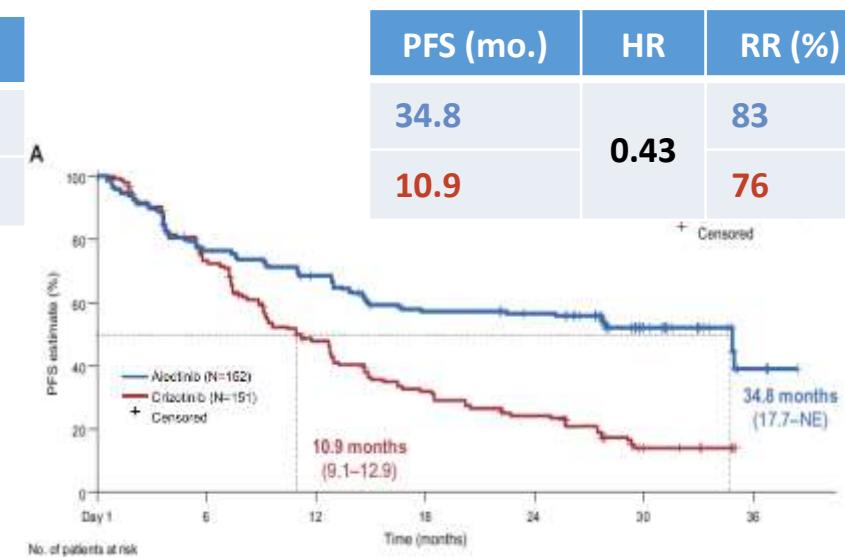
Brigatinib

Lorlatinib

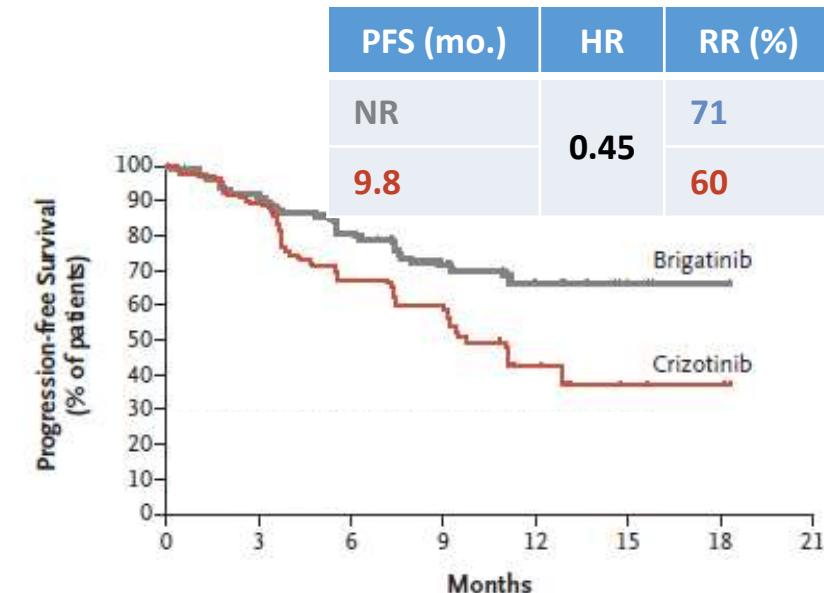
ASCEND-4: Ceritinib vs. CT



ALEX: Alectinib vs. crizotinib



ALTA-1L: Brigatinib vs. CT



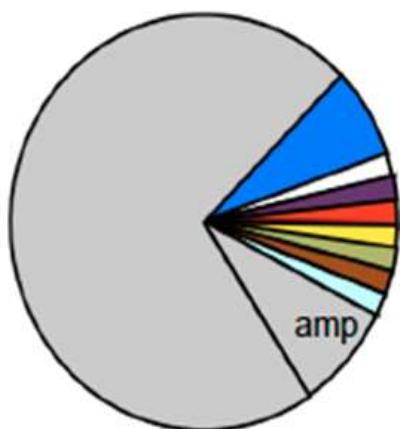
This made 2<sup>nd</sup> generation TKI Standard of Care

# I start with...

What resistance profile I will get?

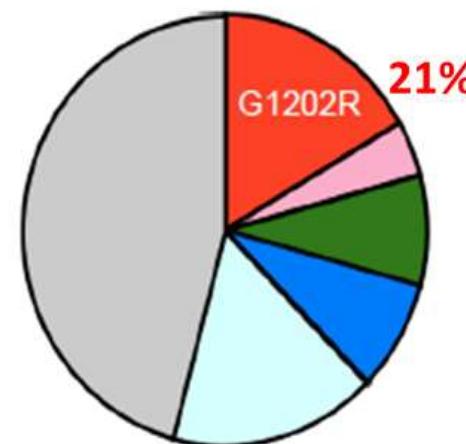
Crizotinib

N=55



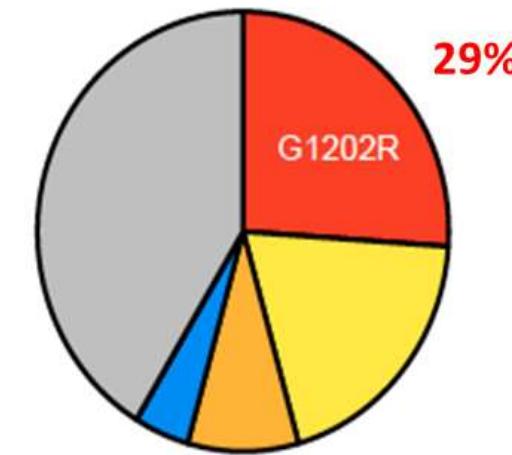
Ceritinib

N=24



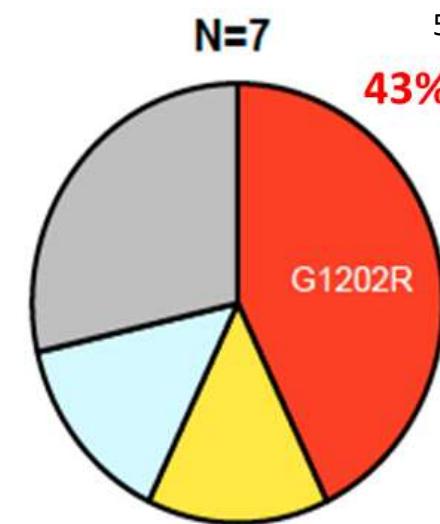
Alectinib

N=46



Brigatinib

N=7



- L1196M/Q
- G1269A
- C1156Y

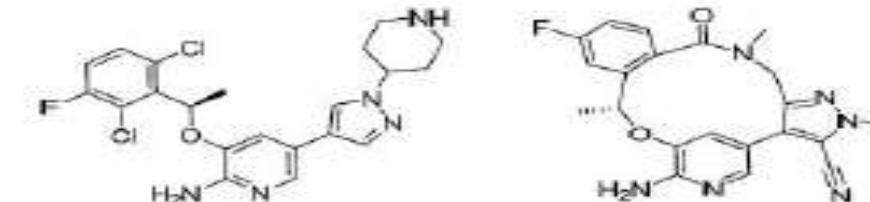
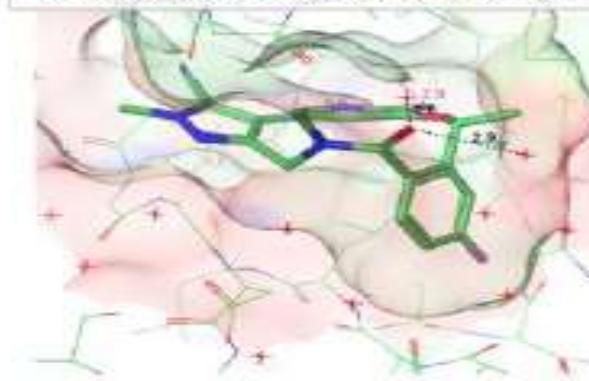
- G1202R
- I1171T/N/S
- S1206Y

- E1210K
- F1174C
- V1180L
- G1202del
- ≥2 ALK mutations
- ALK WT (ALK-independent)

# G1202R is the difficult one

## Lorlatinib

PF-06463922/L1196M-ALK bound structure

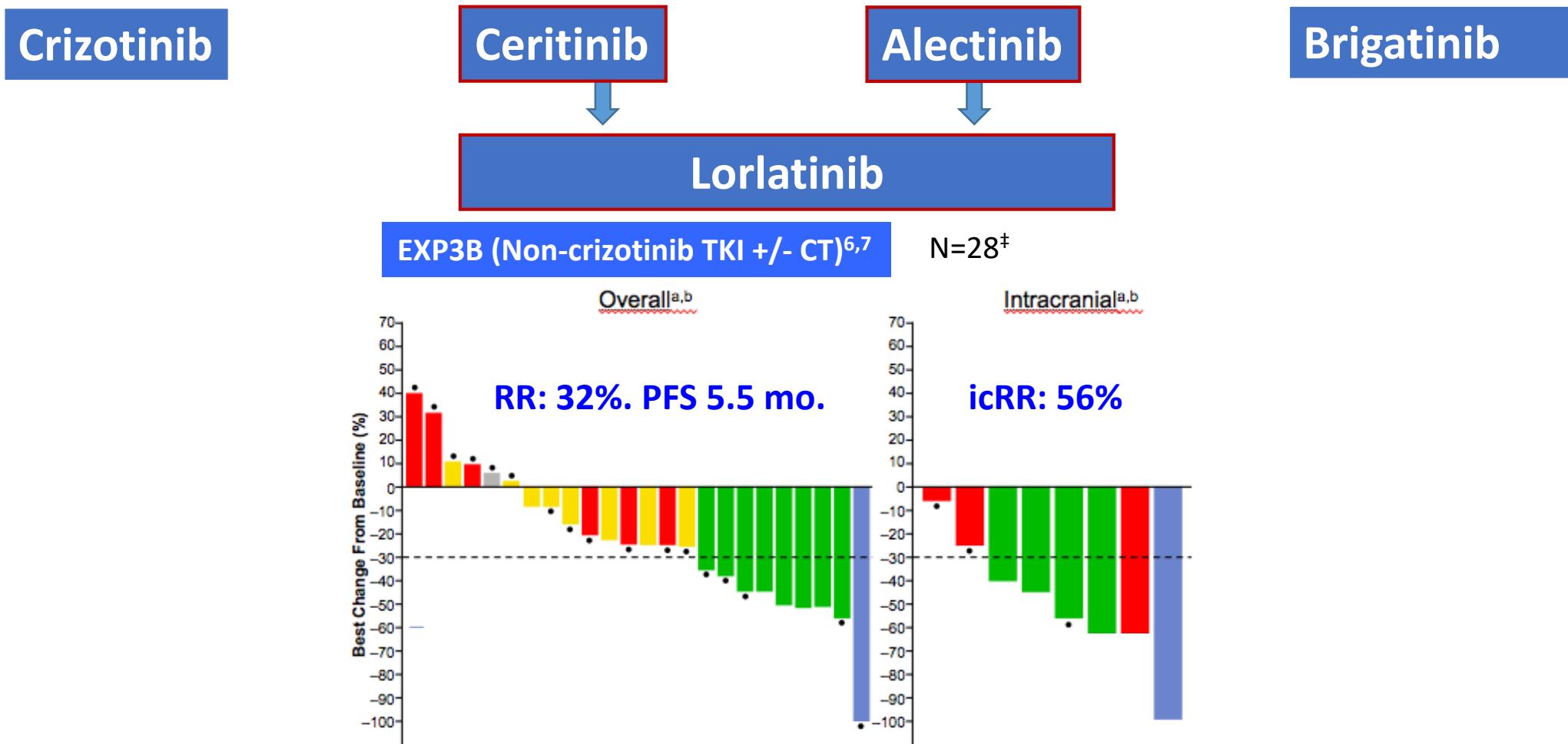


crizotinib

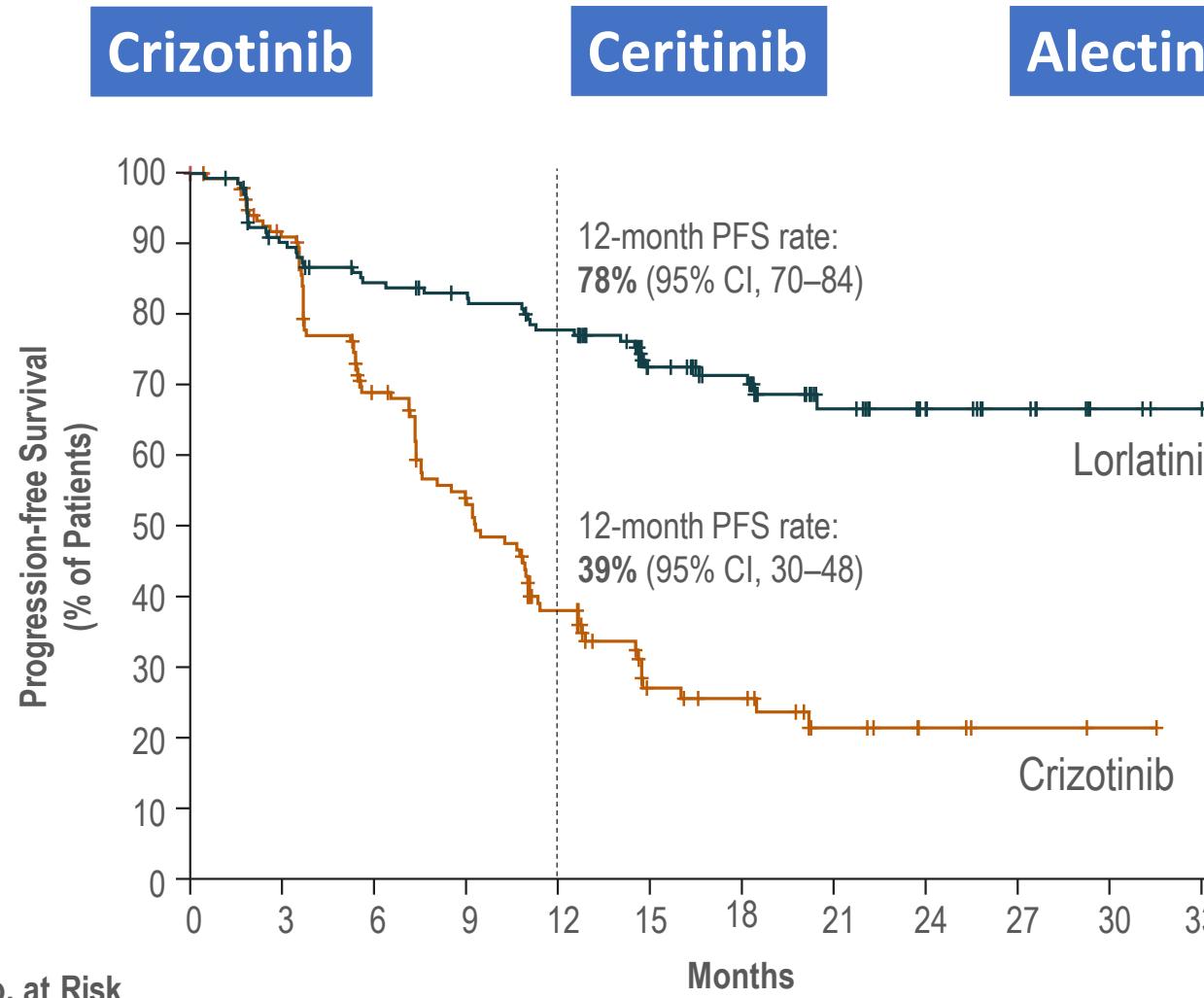
PF-06463922

<i>ALK WT NIH3T3 IC50 (nM)</i>	80	1.5
<i>ALK L1196M NIH3T3 IC50 (nM)</i>	843	21
<b><i>ALK G1202R NIH3T3 IC50 (nM)</i></b>	<b>1148</b>	<b>77</b>
<i>ROS1-CD74 IC50 (nM)</i>	11	0.24
<i>MDR BA/AB</i>	45	1.5

# I start with...



# I start with...



	<b>Lorlatinib (n=149)</b>	<b>Crizotinib (n=147)</b>
<b>Patients with event, n (%)</b>	41 (28)	86 (59)
<b>Median PFS, months (95% CI)</b>	NE (NE–NE)	9.3 (7.6-11.1)
<b>HR (95% CI) 1-sided P value*</b>	0.28 (0.19-0.41)	<0.001

\*By stratified log-rank test.

# I start with...

**Crizotinib**

**Ceritinib**

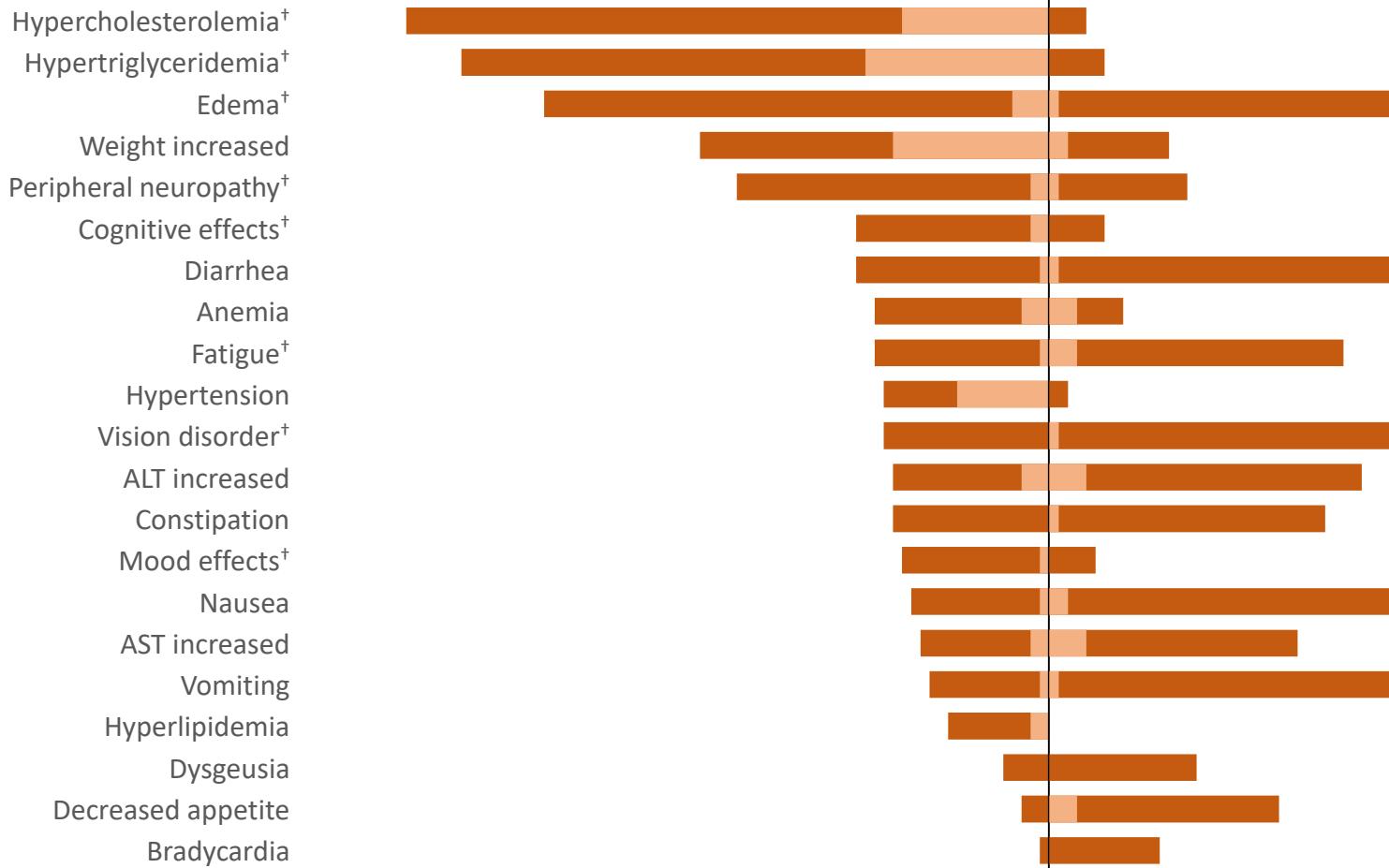
**Alectinib**

**Brigatinib**

**Lorlatinib**

**Lorlatinib (n=149)**

**Crizotinib (n=142)**



Grade 3-4

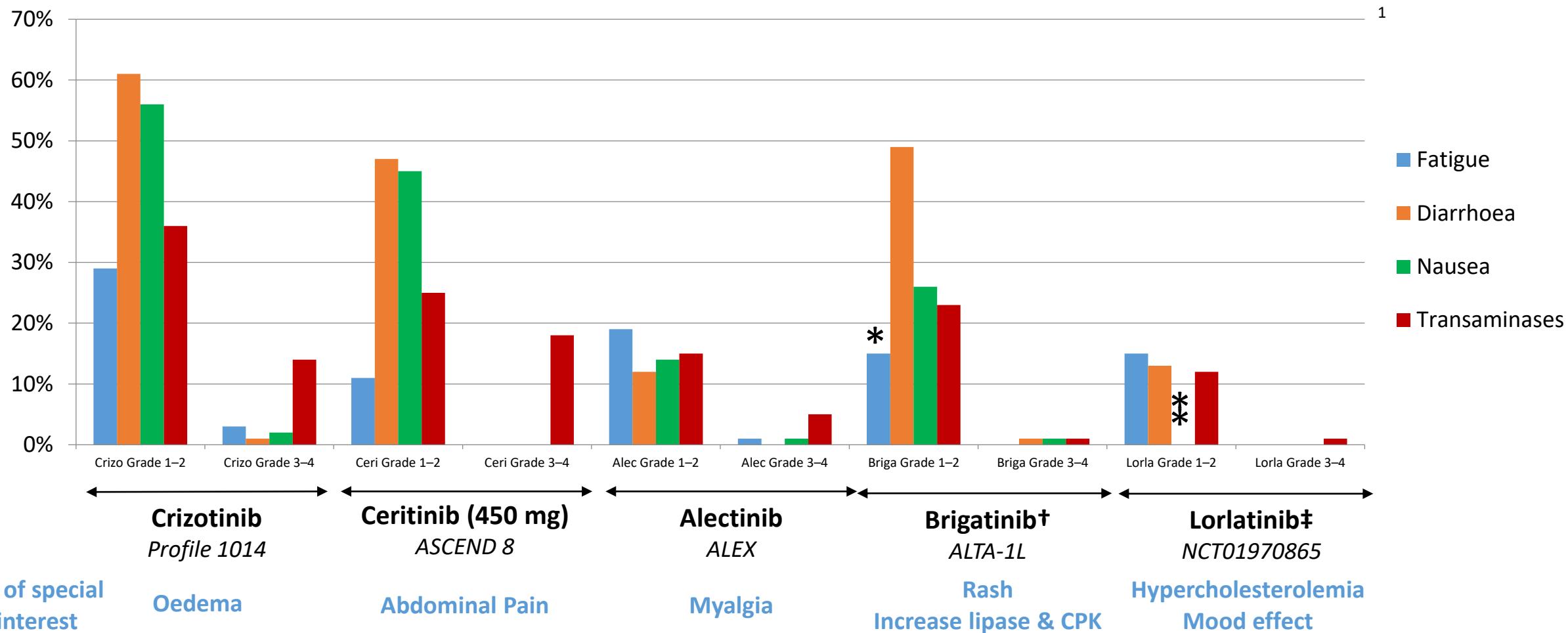
Any grade

Solomon ESMO 2020

<sup>†</sup>Cluster term

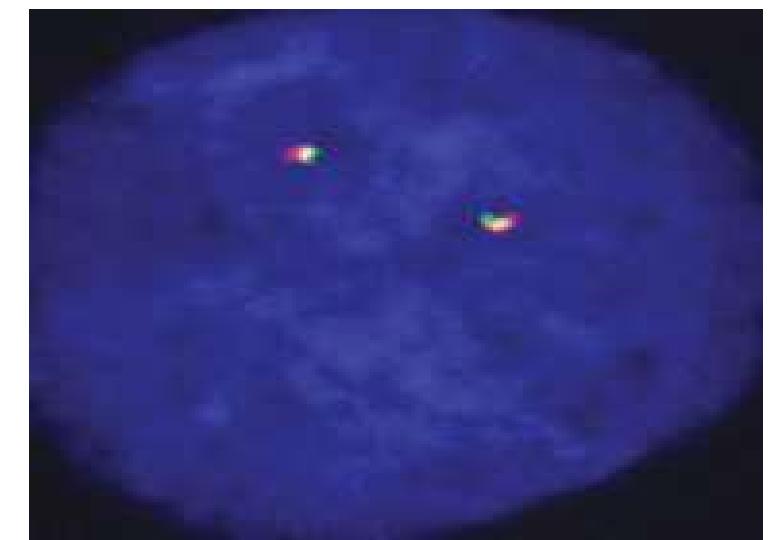
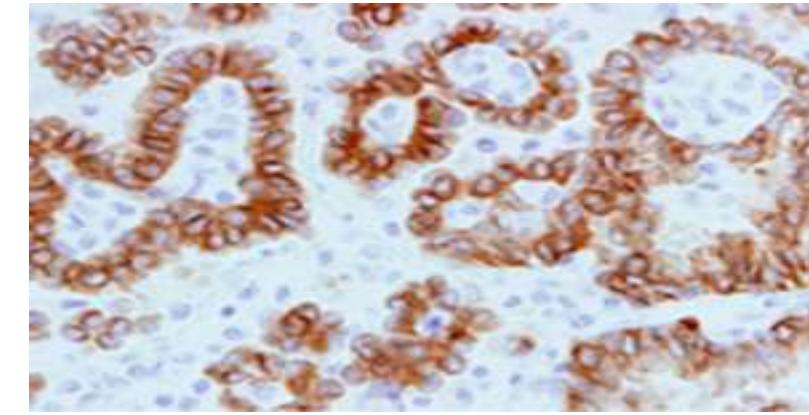
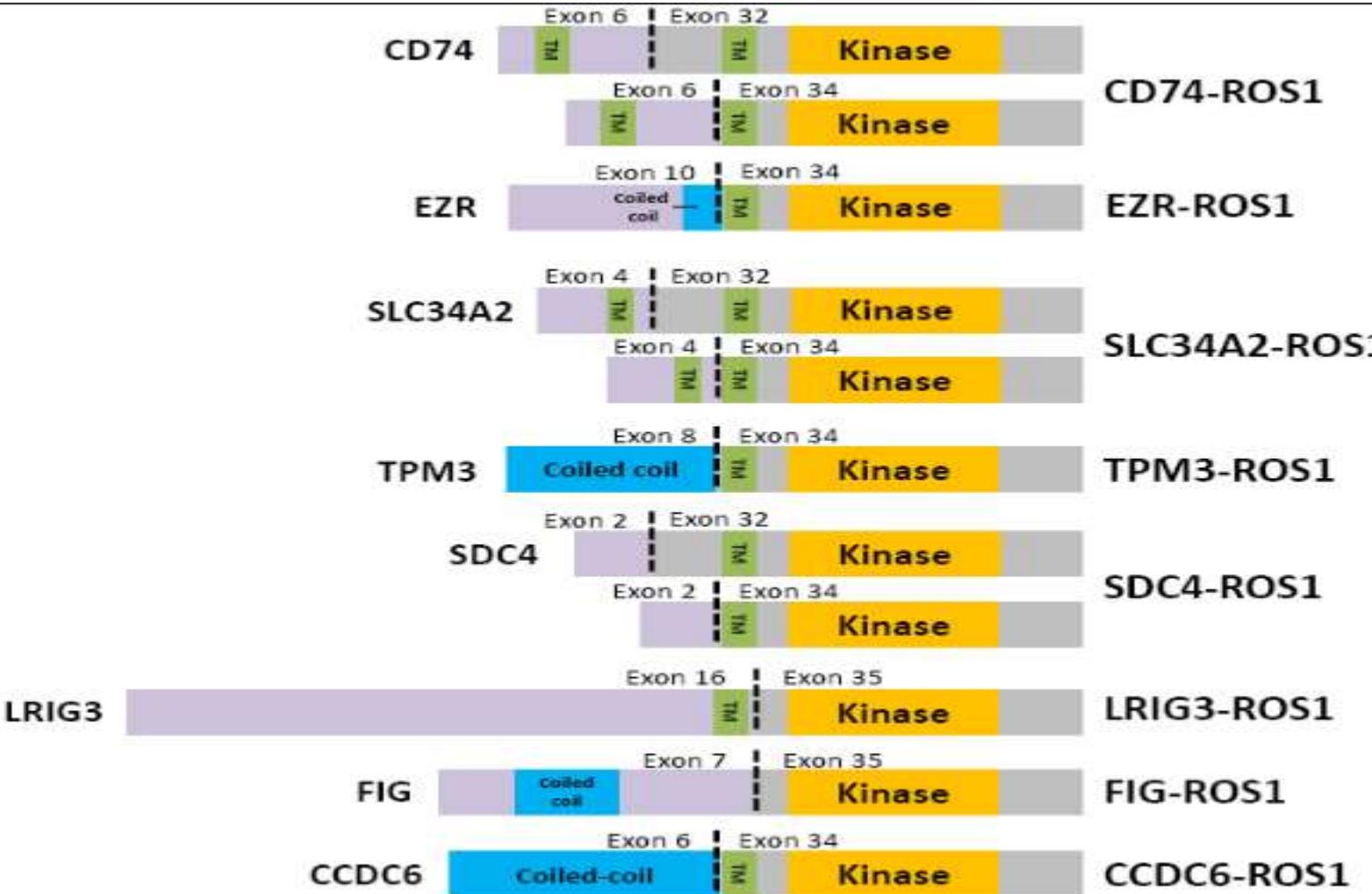
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

# Safety profile of second-generation ALK TKI



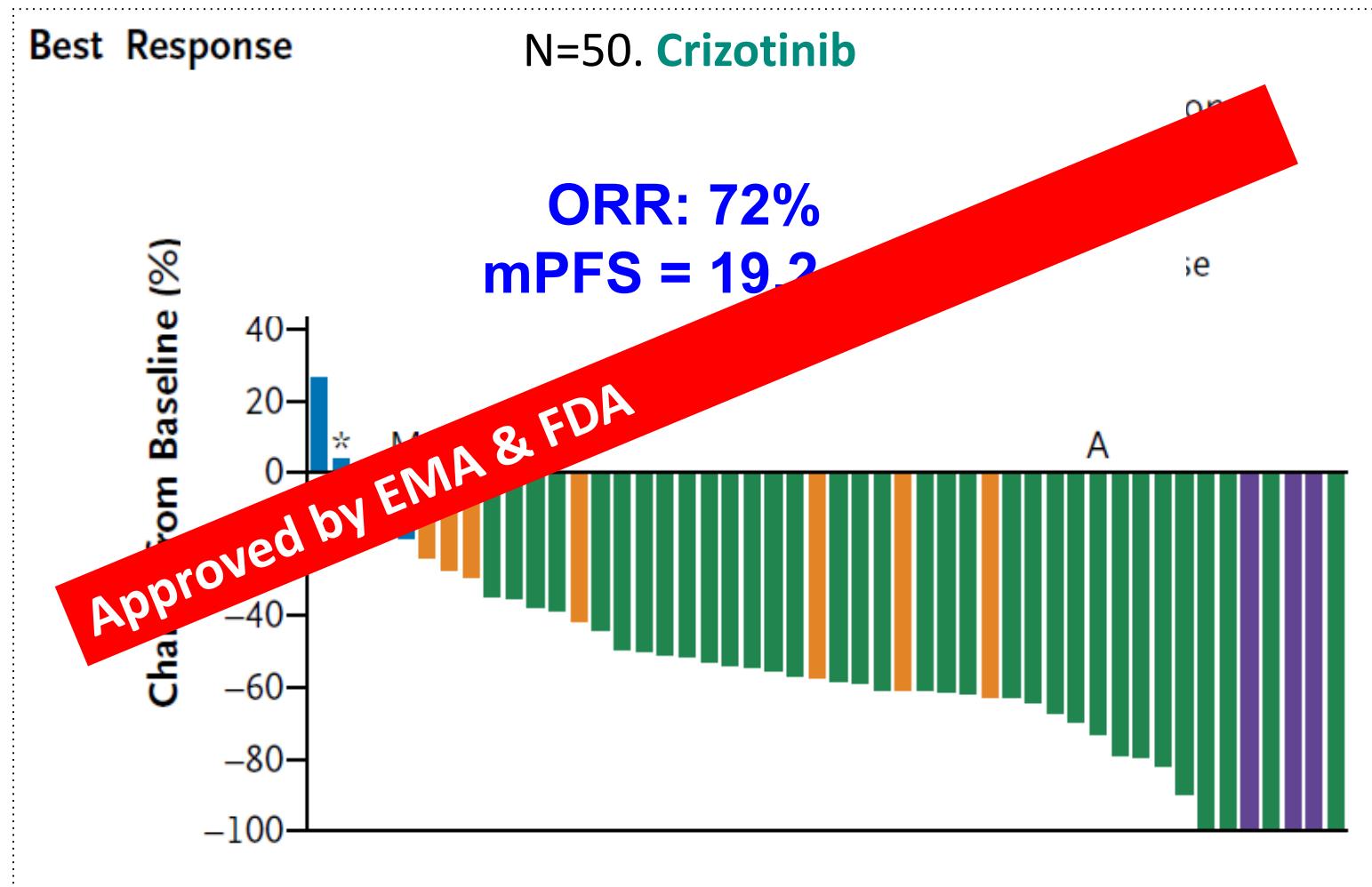
Adapted from M. Perol. Solomon B, et al. N England J Med 2014;341:2167–77. Cho B, et al. J Thorac Oncol 2017;12(9):1357–67, Peters NEJM 2017;377(9):829–38; Camidge D. Presented at WCLC 2018, Toronto, Canada, 23–26 September, 2018; Besse B, et al. J Clin Oncol 2018;36(suppl 15):9032

# ROS1



1% of NSCLC = 15 000 people worldwide, around 200 to 300 in France/year

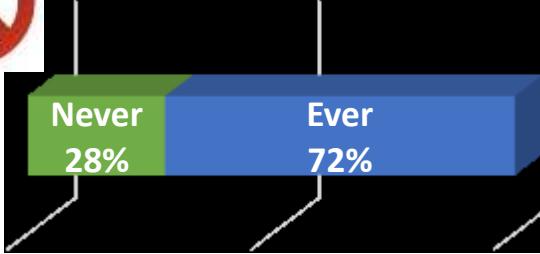
# ROS1 rearrangement (~2%)



# BRAF<sup>V600E</sup> in NSCLC : ID



## Smoking status

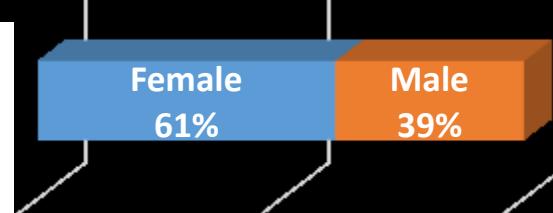


## Median Age

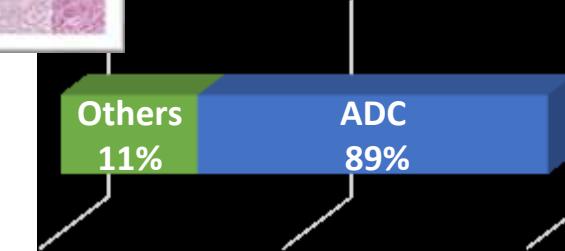
67



## Sex Ratio



## Non-Squamous



## PD-L1 ≥1%

75%

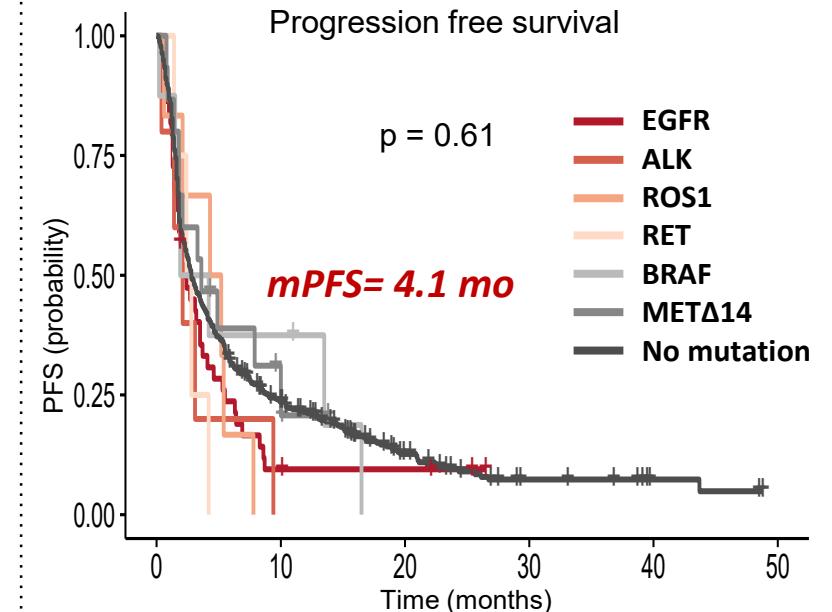


## Median TMB

5.4%

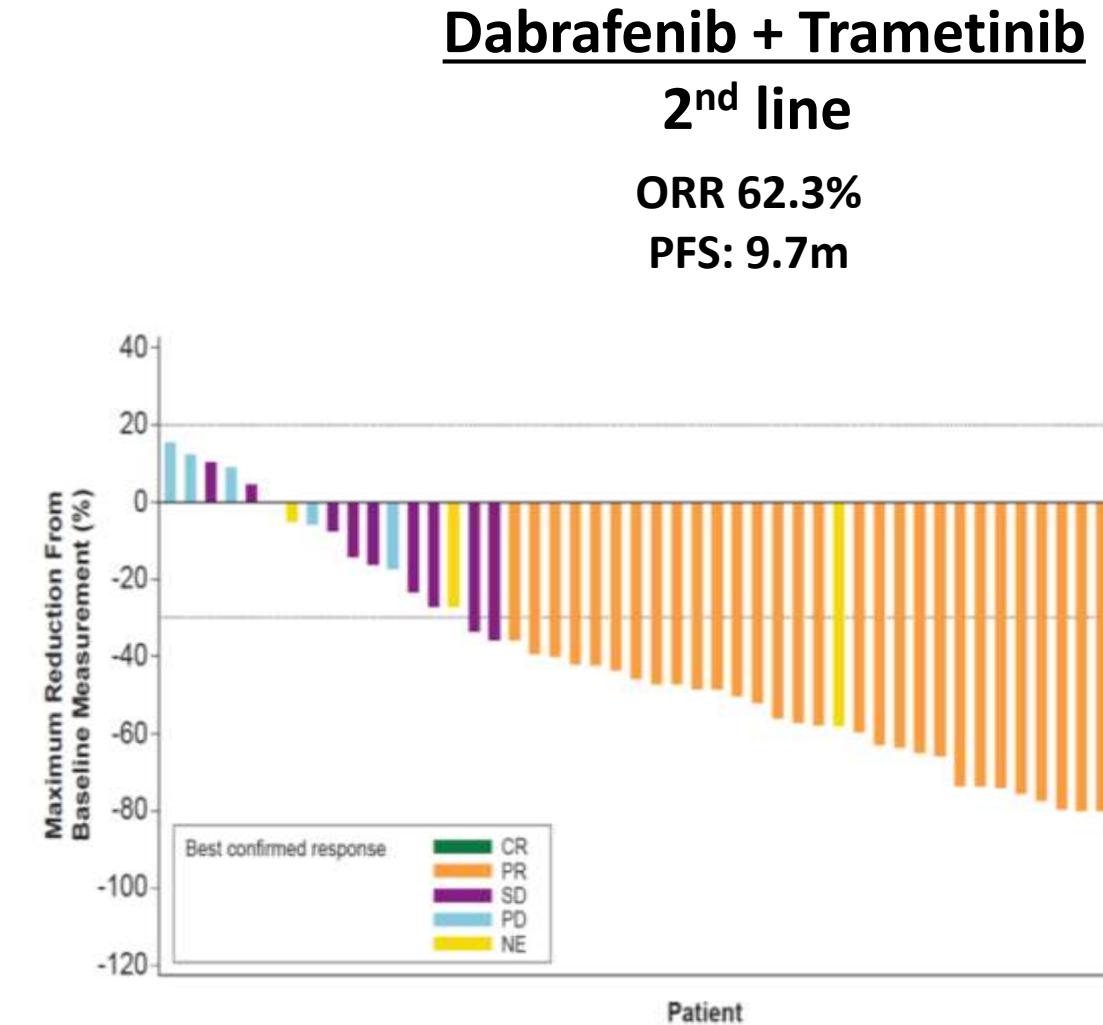
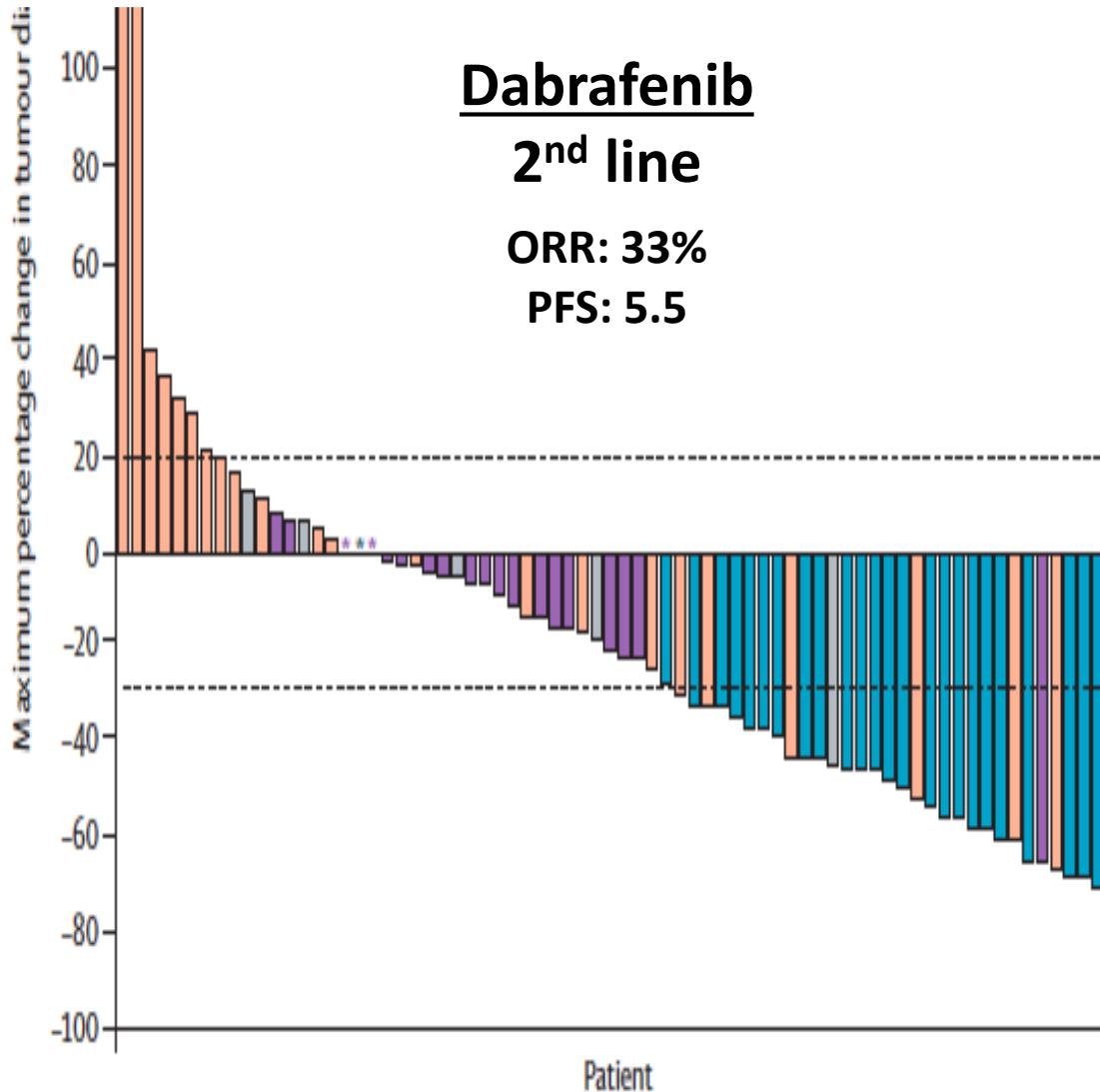


## Prognostic value



Low rate brain Mets at diagnosis

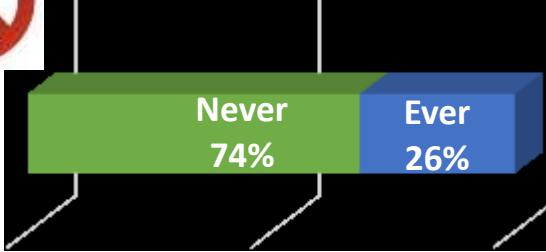
# BRAF or BRAF + MEK inhibitors?



# RET fusion in NSCLC ID



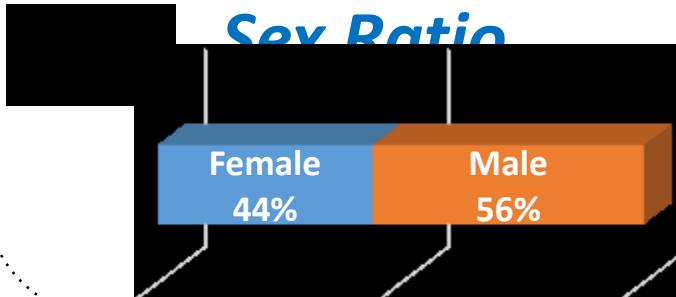
*Smoking status*



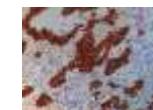
*Median Age*

**61**

*Sex Ratio*



*Non-Squamous*



*PD-L1 ≥1%*

67%



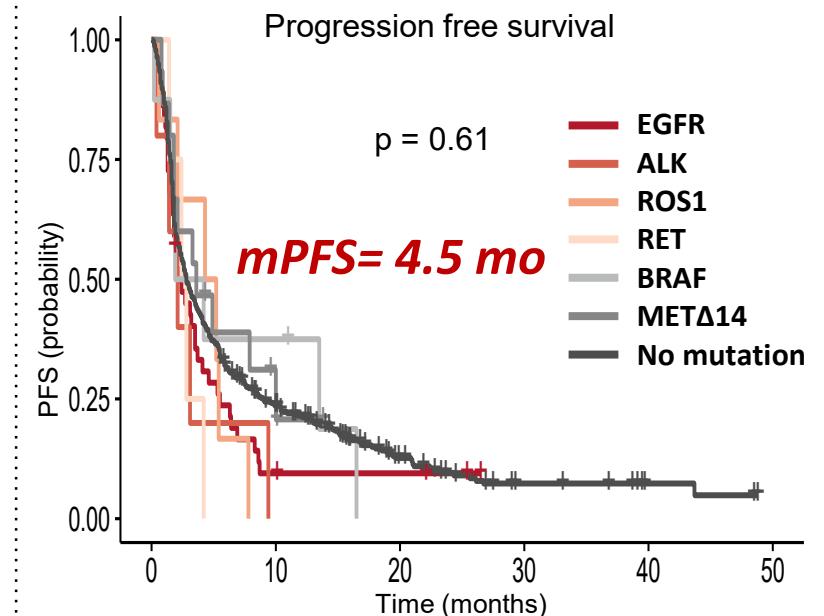
*Median TMB*



*Low*



*Prognostic value*

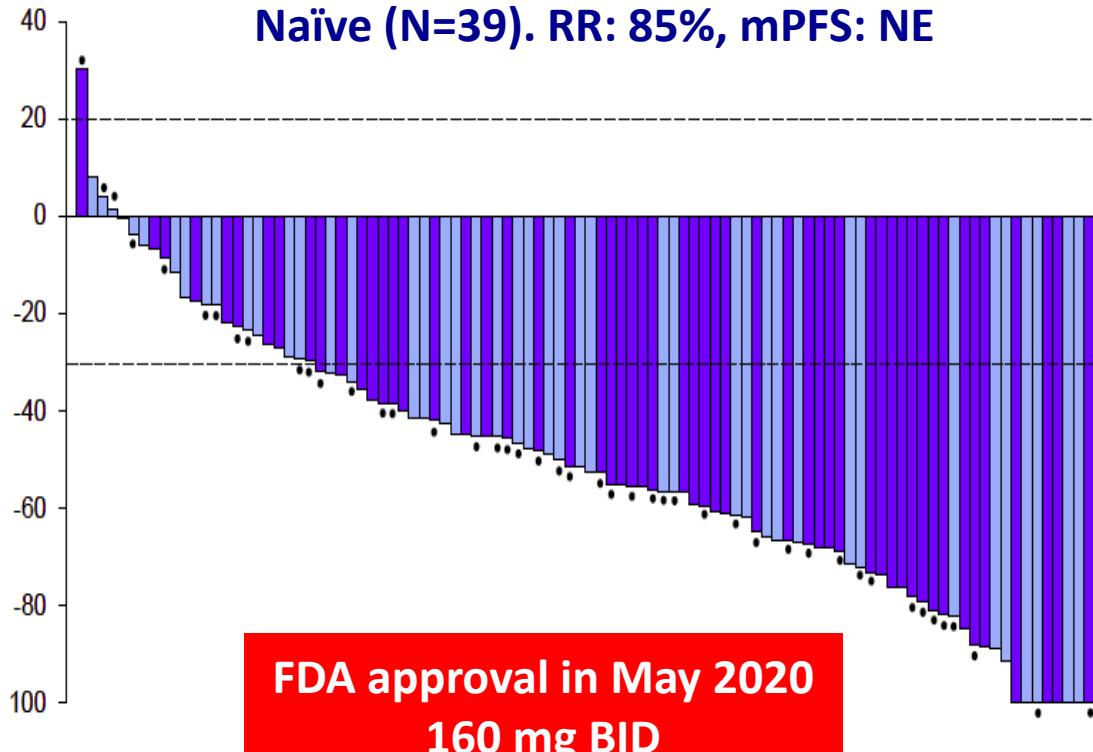


*18% CNS mets at Diagnosis*

# Specific RET inhibitors

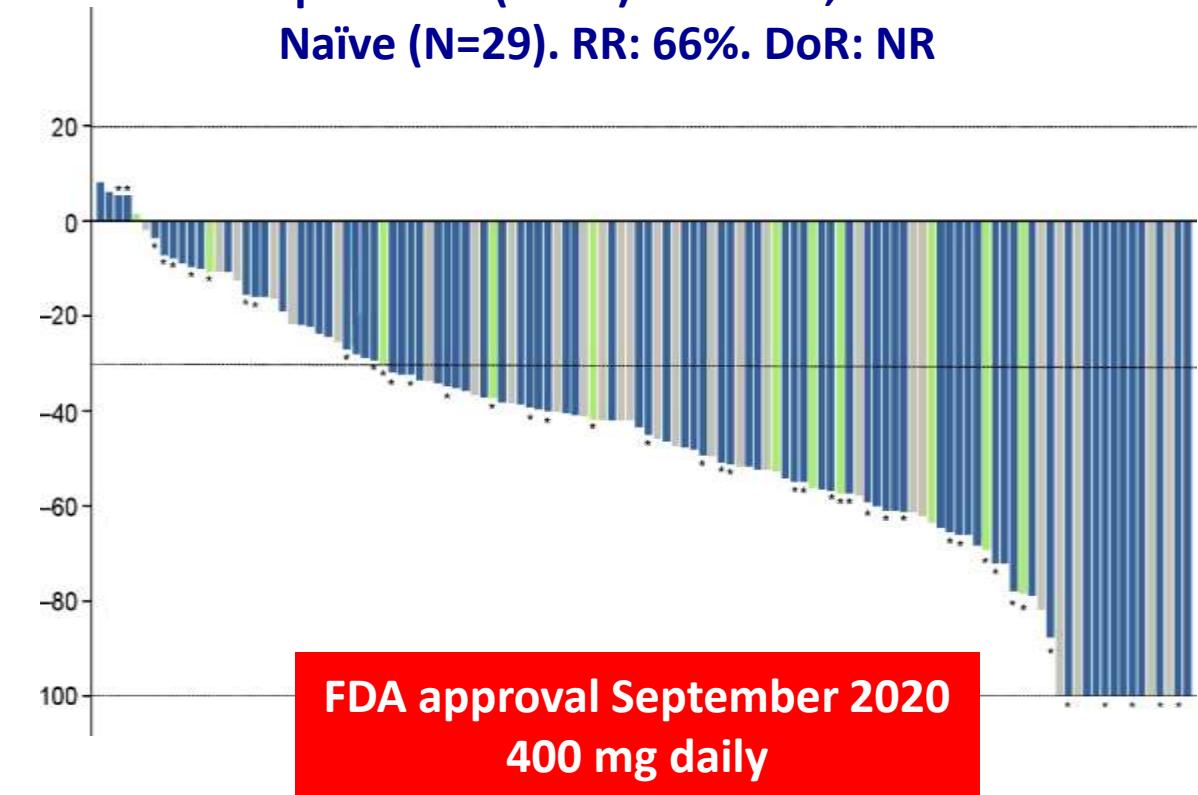
## Selpercatinib (LOXO-292): LIBRETTO-1 trial

Prior platinum (N=105). RR: 64%, mPFS: 17 mo.  
Naïve (N=39). RR: 85%, mPFS: NE



## Pralsetinib (BLU-667): ARROW trial

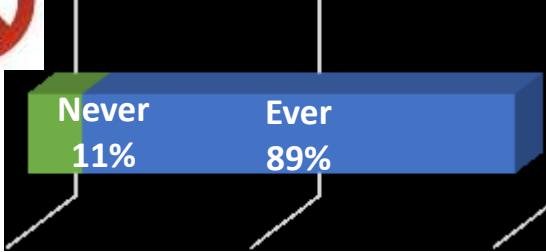
Prior platinum (N=92). RR: 55%, DoR: NR  
Naïve (N=29). RR: 66%. DoR: NR



# KRAS G12C mutation in NSCLC ID



## Smoking status

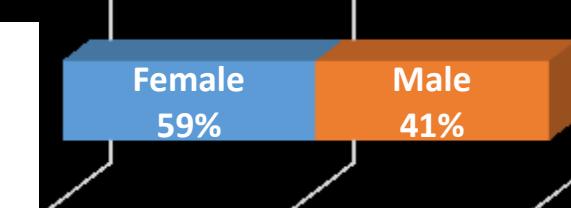


## Median Age

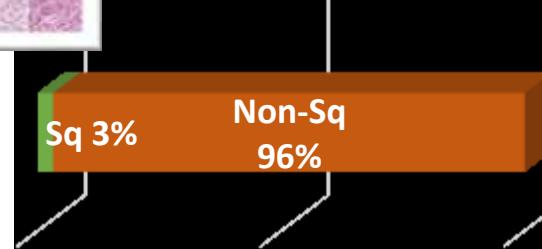
65



## Sex Ratio

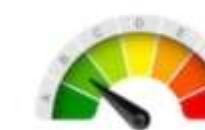


## Non-Squamous



## PD-L1 ≥1%

29%

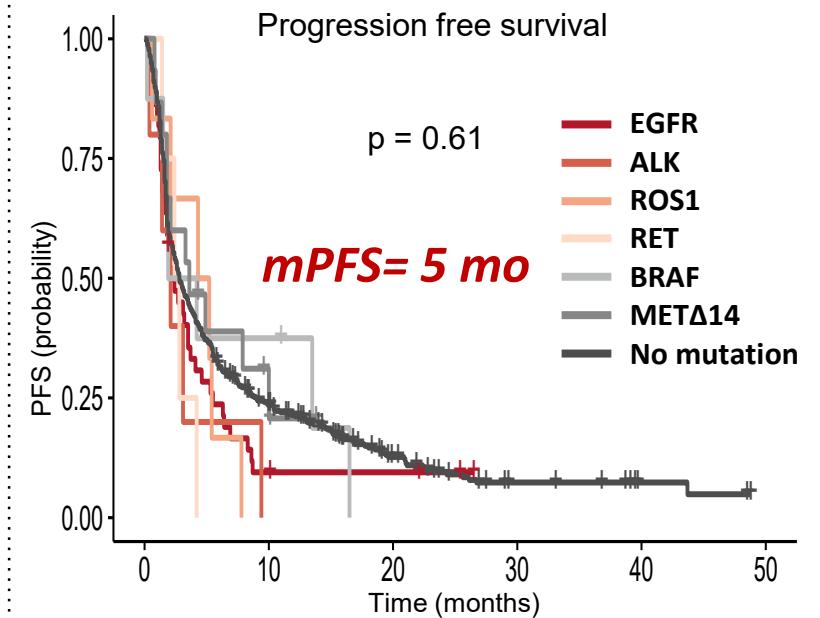


## Median TMB

9.8%

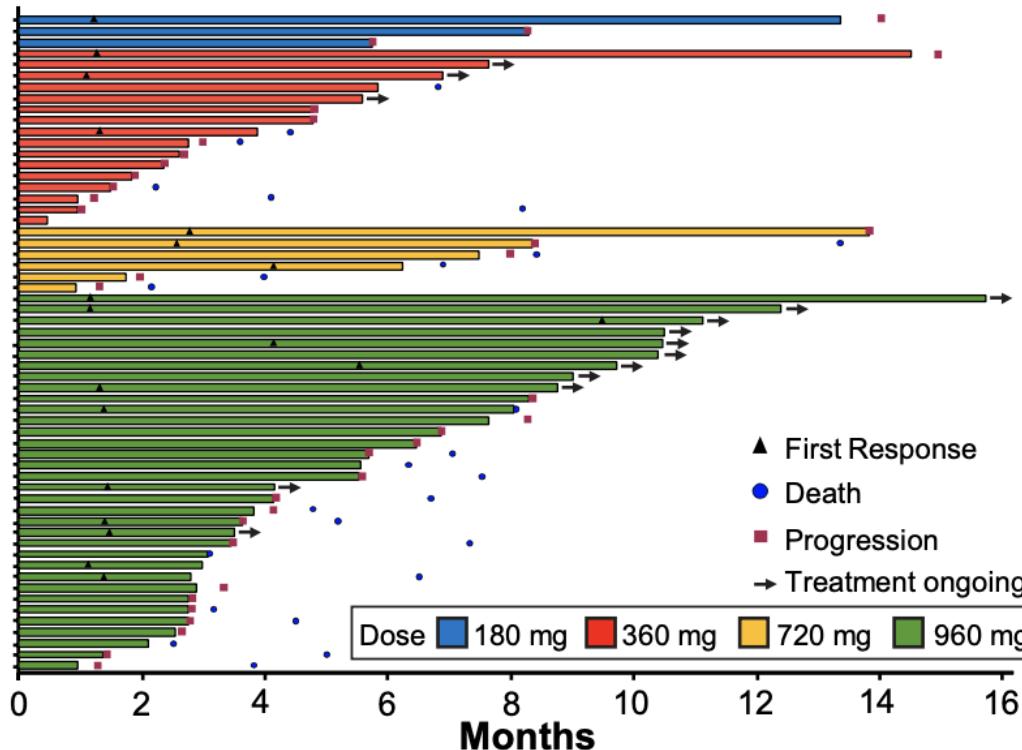


## Prognostic value



# Sotorasib (AMG 510)

Patients with NSCLC Receiving Sotorasib



**Confirmed PR, n = 19**

**Duration of response\***

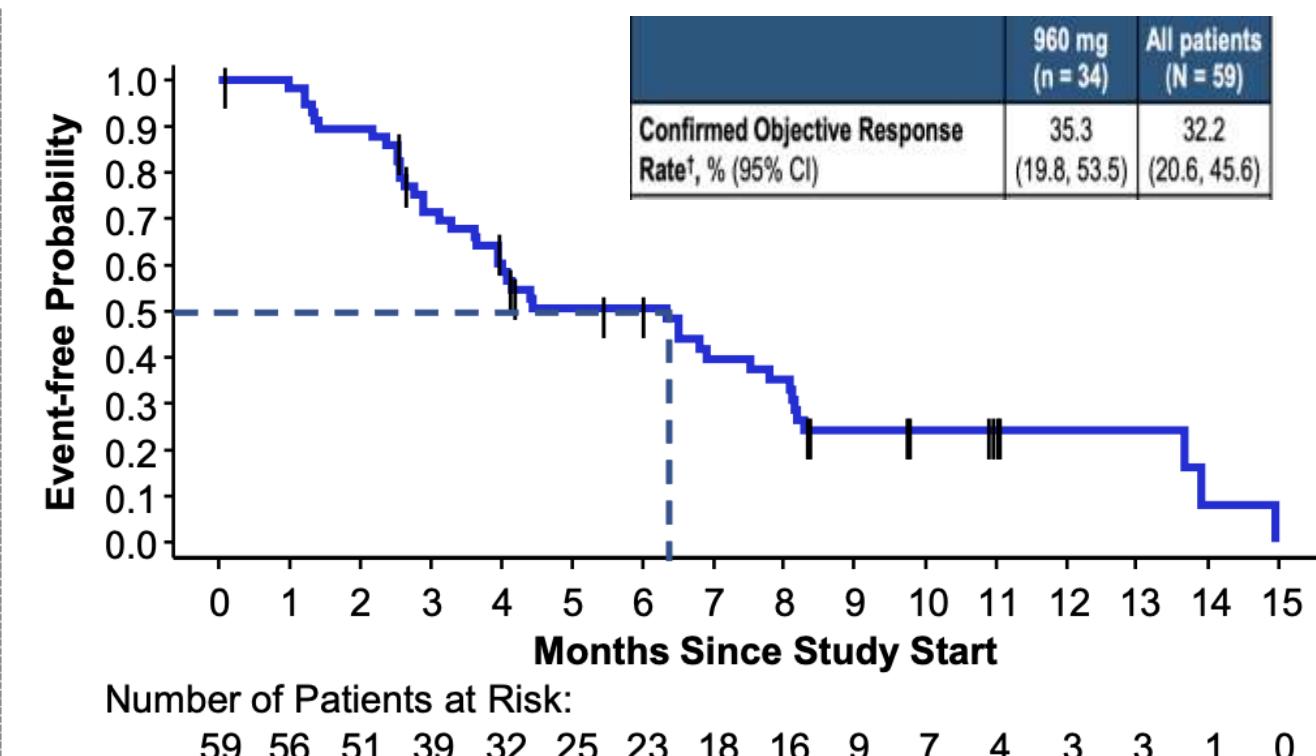
Median of 10.9 (1.1+ to 13.6) months

10/19 responders still in response†

**Patients with SD, n = 33**

**Duration of stable disease‡**

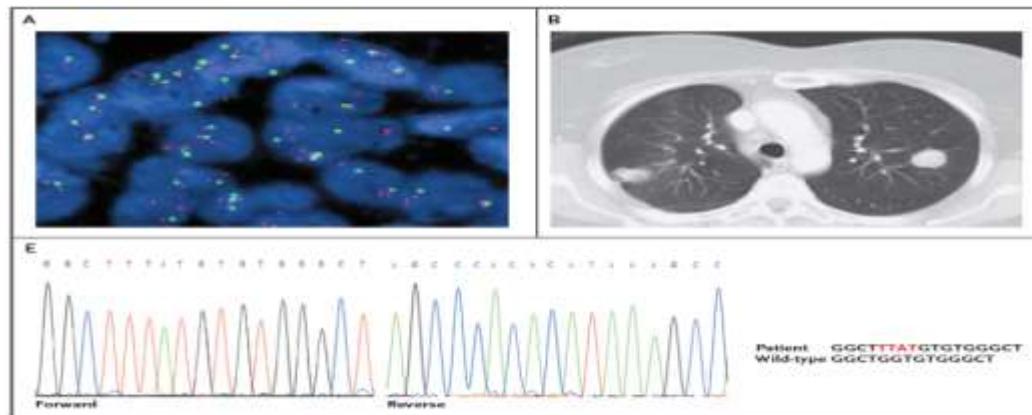
Median of 4.0 (1.4 to 10.9+) months



**Median PFS: 6.3 (range 0.0+ to 14.9) months**

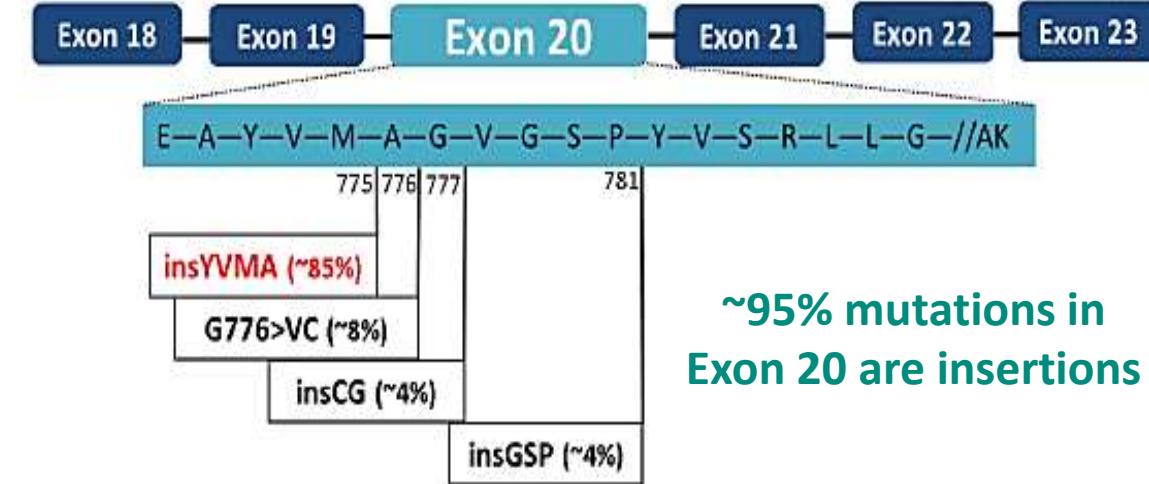
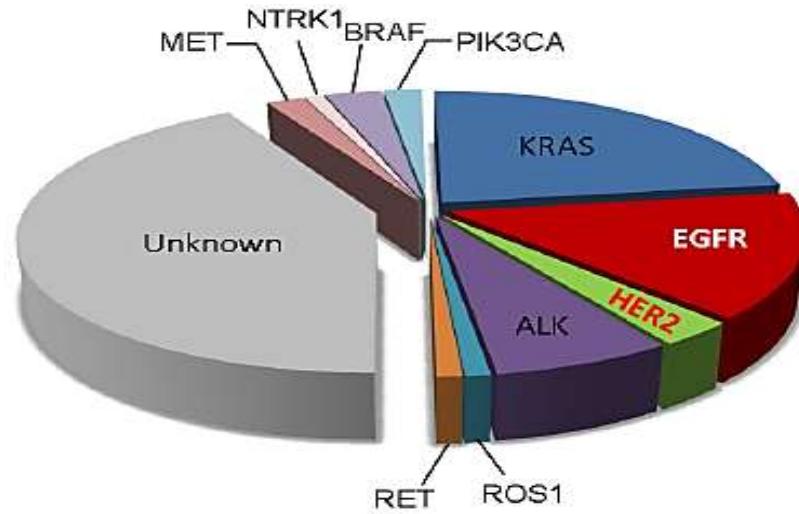
# HER2 aberrations in NSCLC

HER2 in NSCLC	Frequency
Overexpression (IHC 2+ and 3+)	15–30%
Overexpression (IHC 3+ only)	2–6%
Amplification (ISH)	2–6%
Mutations	1–5%



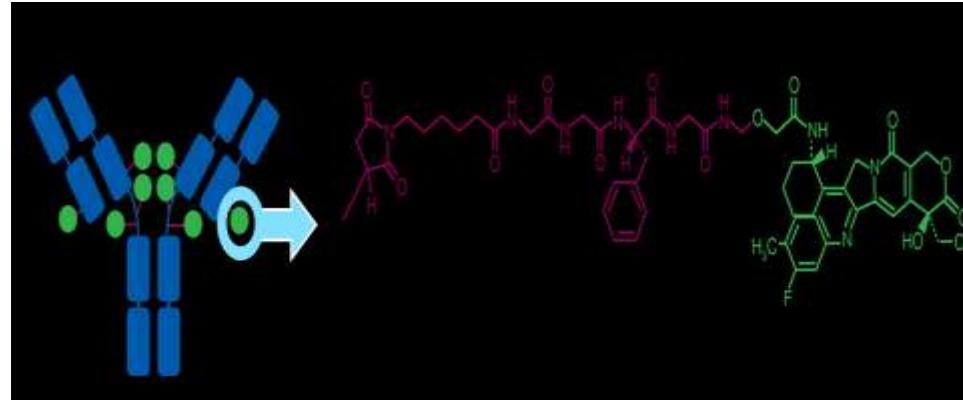
**Mutation and amplification are not associated**

BM in 47% of HER2-mutant lung cancers (20% baseline)



**~95% mutations in Exon 20 are insertions**

# T-DXd: Destiny Lung01 phase II Trial



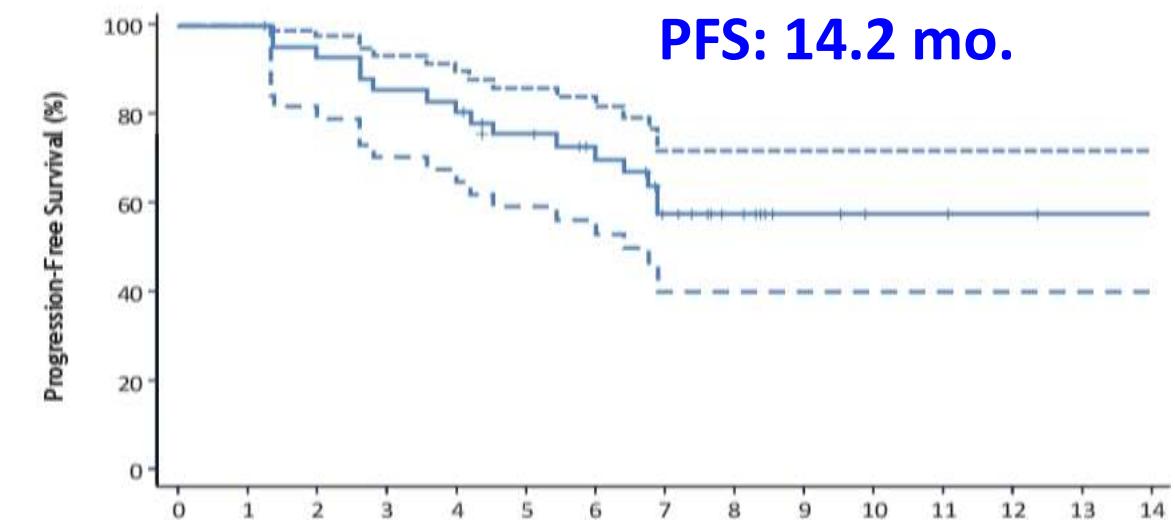
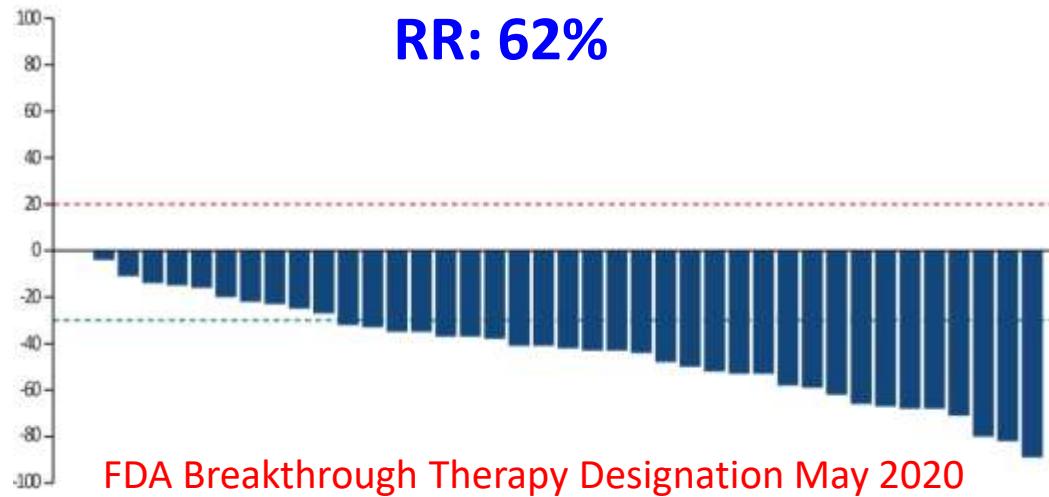
## Patients

- Unresectable/metastatic nonsquamous NSCLC
- Relapsed/refractory to standard treatment
- HER2-expressing or HER2-activating mutation<sup>a</sup>
- No prior HER2-targeted therapy, except pan-HER TKIs

**Cohort 1 (n = 42)**  
HER2 expressing (IHC 3+ or IHC 2+)

**Cohort 2 (n = 42)**  
HER2 mutated

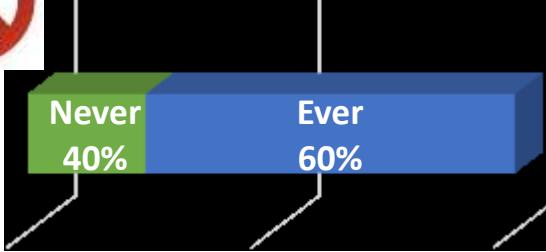
T-DXd 6.4 mg/kg q3w



# MET 14mut in NSCLC ID



## Smoking status

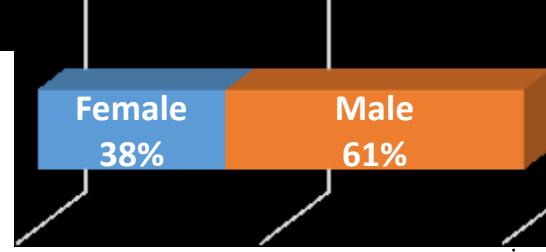


## Median Age

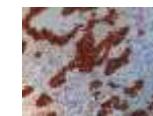
**73**



## Sex Ratio



## Non-Squamous



## PD-L1 $\geq 1\%$

**52%**

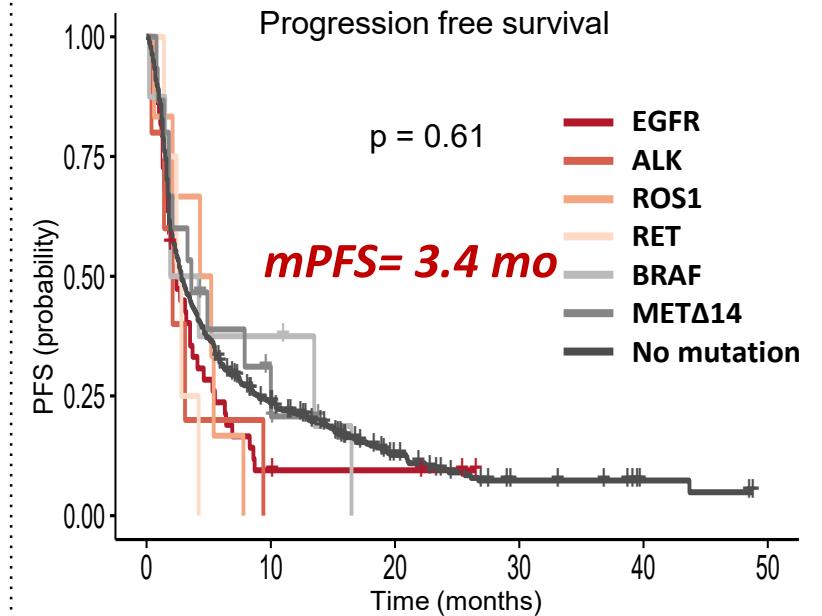


## Median TMB

**Low**



## Prognostic value



**17% CNS mets at Diagnosis**

# MET TKI in METex14 NSCLC

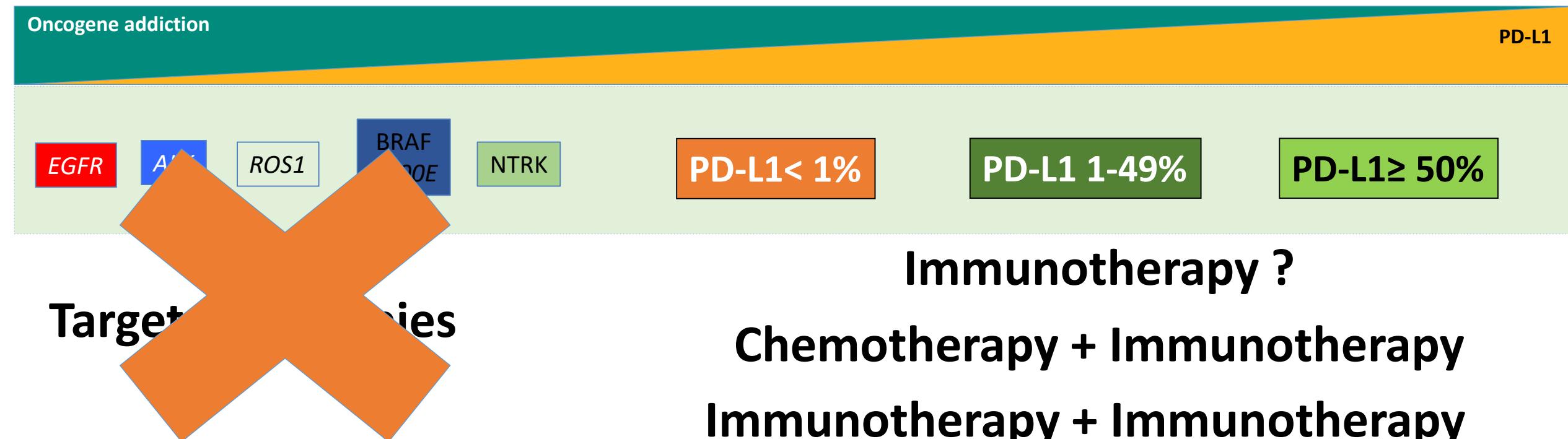
	Dose	Line	N	RR (%)	PFS (mo.)
<b>CRIZOTINIB</b> (PROFILE 1001)	250 mg BID	<b>Naïve</b>	24	25	7.3
		≥ 2 <sup>nd</sup> L	41	37	
<b>CAPMATINIB</b> (GEOMETRY)	400 mg BID	<b>Naïve (cohort 5B)</b>	28	68	12.4
		2 <sup>nd</sup> L (cohort 6)	27	48	8.1
		2 <sup>nd</sup> /3 <sup>rd</sup> L (cohort 4)*	69	41	5.4
<b>TEPOTINIB</b> (VISION)	500 mg QD	<b>Naïve</b>	43	44	8.5
		2 <sup>nd</sup> L	33	48.5	
		3 <sup>rd</sup> L	23	48.2	
<b>SAVOLITNIB</b>	600 mg QD (≥ 50 Kg)	<b>Naïve</b>	28	46	5.6
	400 mg QD (< 50 Kg)	Pre-treated	42	41	13.2

\*88% chemotherapy, 26% ICI, No previous MET inhibitors

Drilon- Nature Med 2002 \* Wolf –NEJM 2020 \* Garon – AACR 2020 \* Groen –ASCO 2020 \* Paik- NEJM 2020 \* Lu – ASCO 2020

Courtesy of Jordi Remon

# New treatment paradigm in NSCLC



Algorithm by Jordi Reamon

Modified from Jordi Reamon

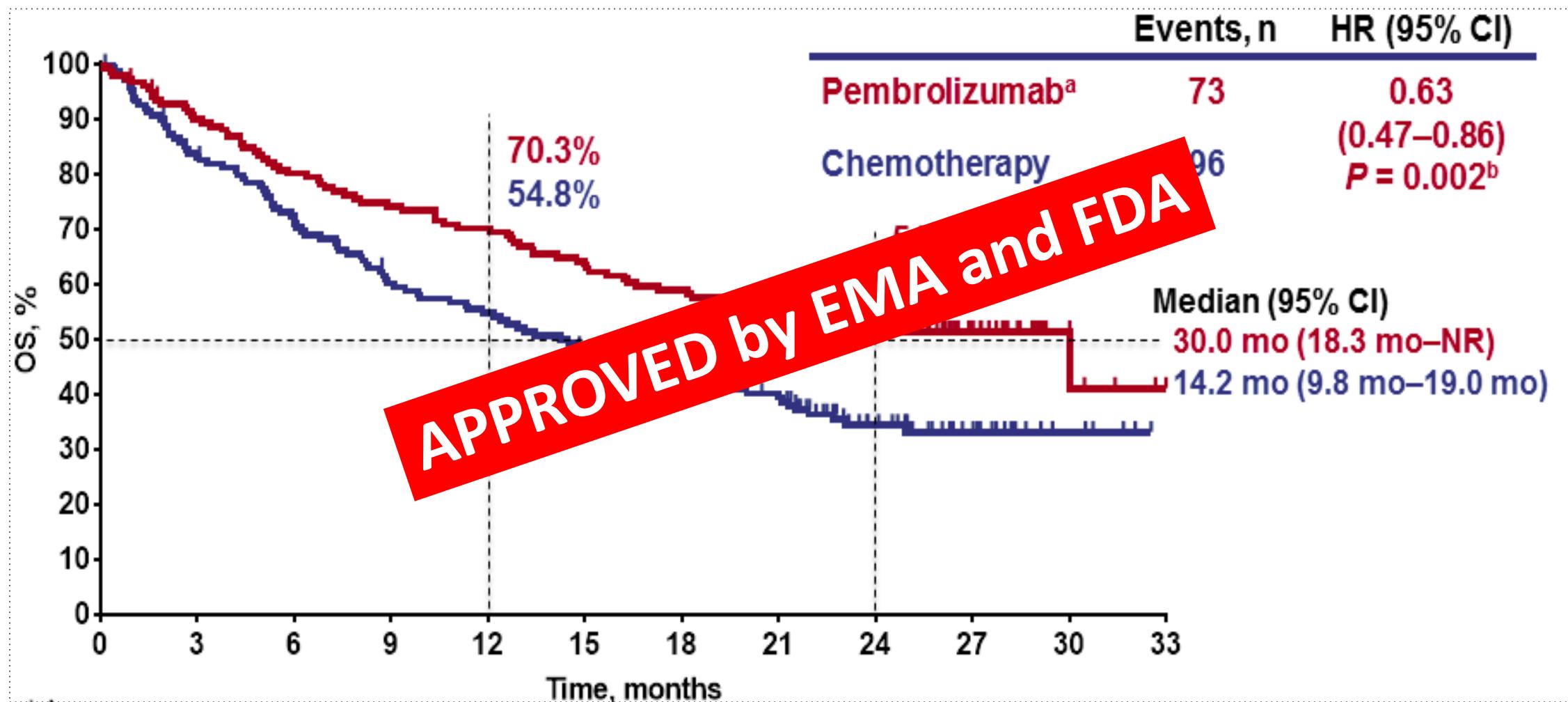
# PD-L1 IHC

## *Is still the king*



**PD-L1 $\geq$  50%**

# PD-L1 $\geq$ 50% or high Pembrolizumab 1st line (KEYNOTE 024)

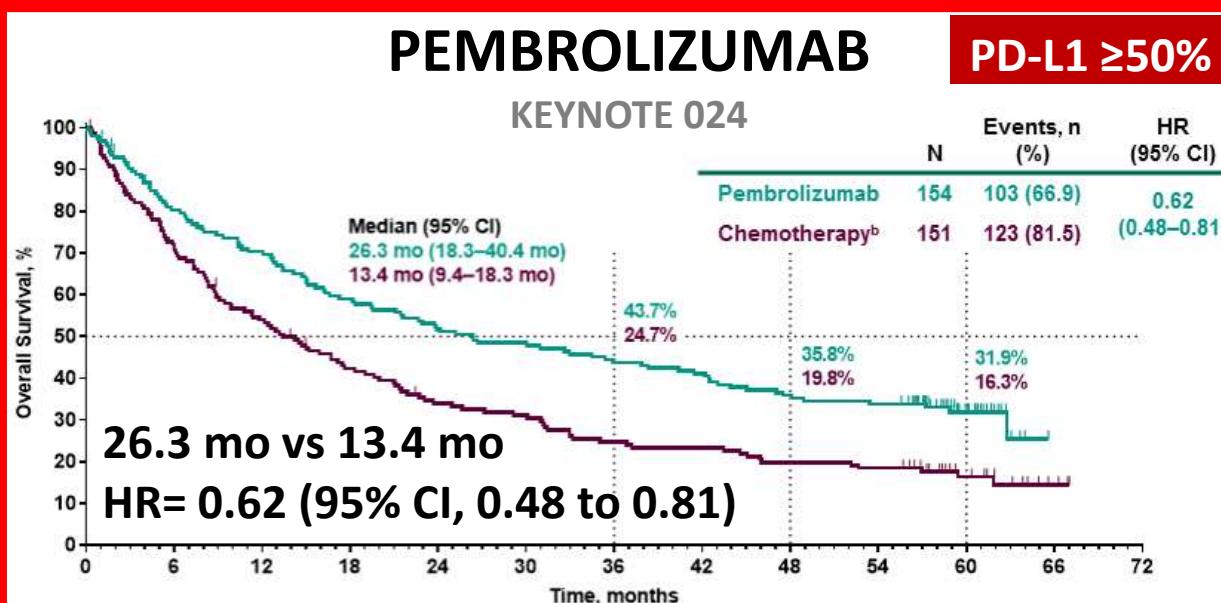


# PD-L1 $\geq$ 50% or high : First-Line single agent IO

## PEMBROLIZUMAB

KEYNOTE 024

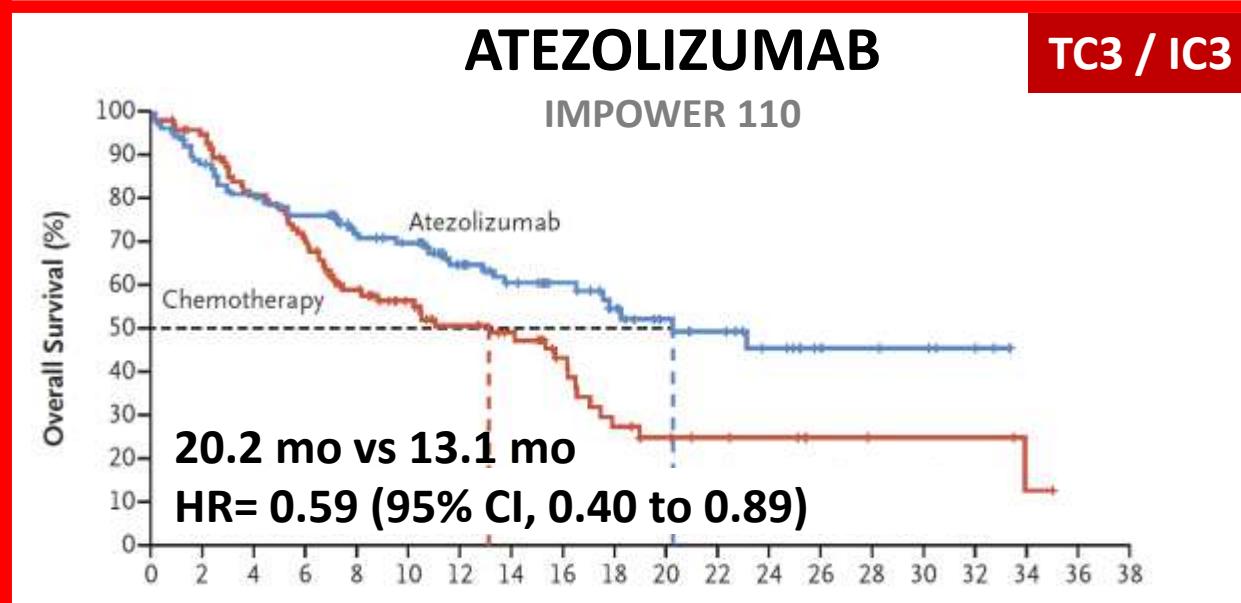
PD-L1  $\geq$ 50%



## ATEZOLIZUMAB

IMPOWER 110

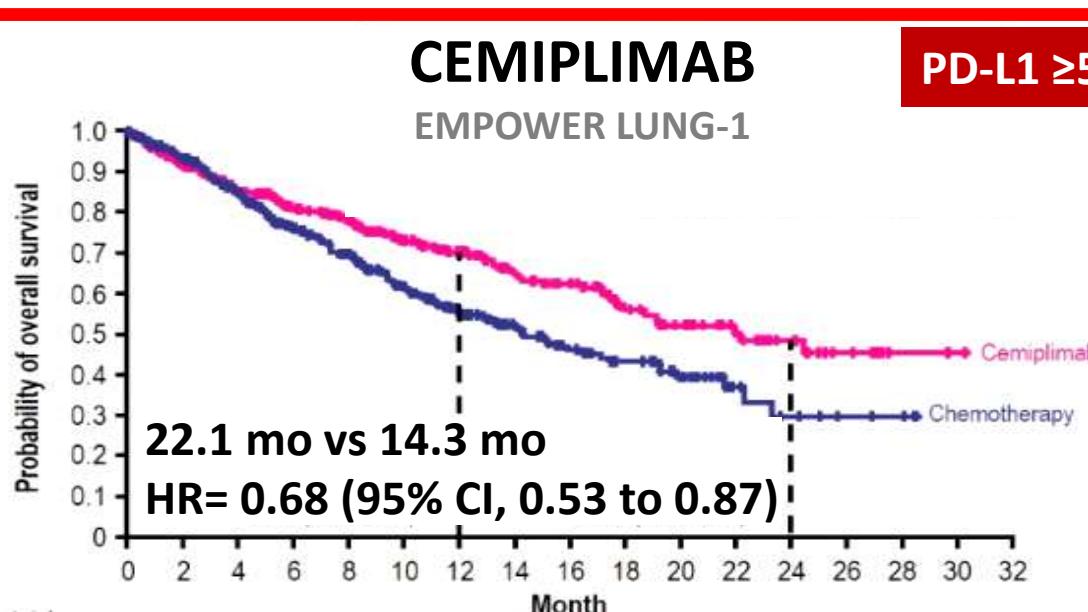
TC3 / IC3



## CEMIPPLIMAB

EMPOWER LUNG-1

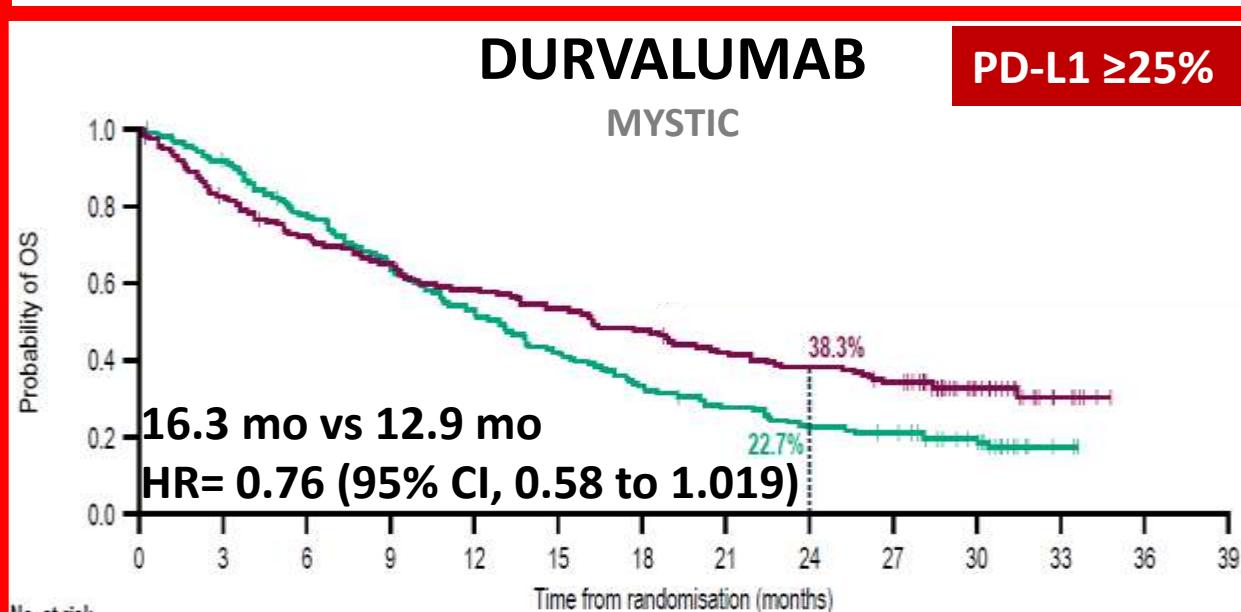
PD-L1  $\geq$ 50%



## DURVALUMAB

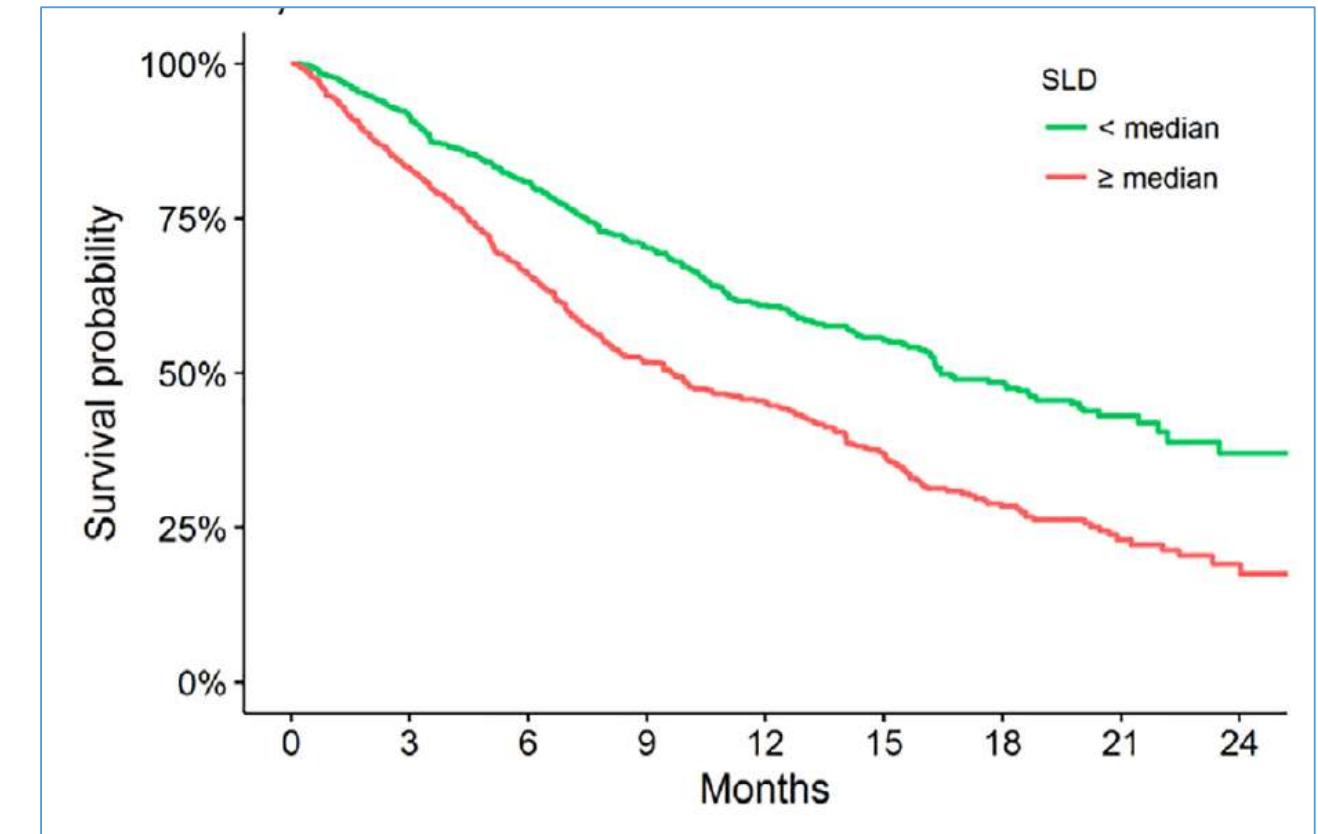
MYSTIC

PD-L1  $\geq$ 25%



# IO efficacy and Tumor burden evaluated through RECIST target size

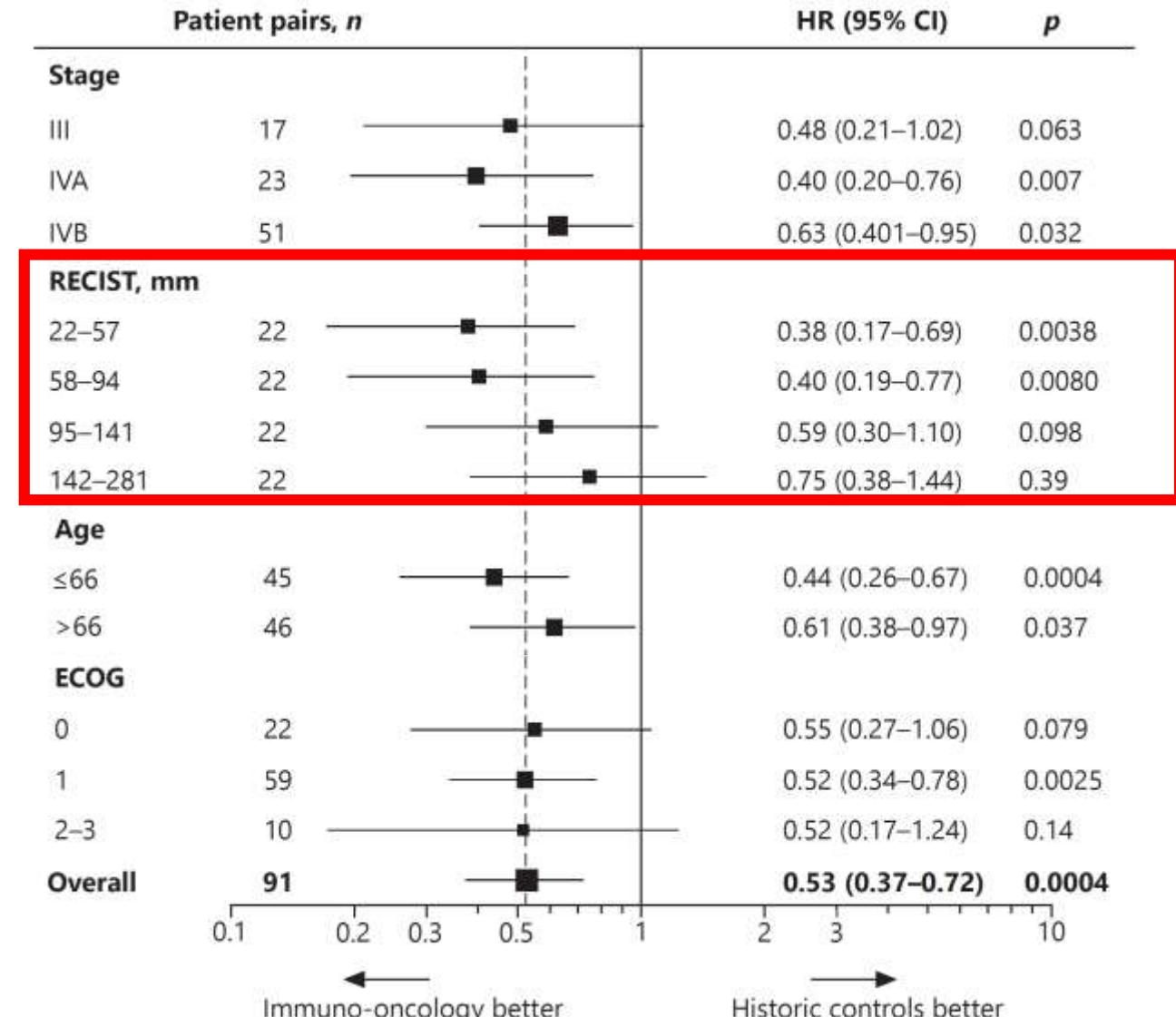
- Secondary analysis pooled individual-participant data from
  - OAK (NCT02008227, July 7, 2016 data cutoff),
  - POPLAR (NCT01903993, May 8, 2015 data cutoff),
  - BIRCH (NCT02031458, May 28, 2015 data cutoff)
  - FIR (NCT01846416, January 7, 2015 data cutoff).
- All analyses were based upon patients with NSCLC who received atezolizumab treatment.
- N=1461 pts
- Baseline SLD is an independent predictor of survival outcomes**



SLD = sum of longest diameters of target lesions.

# IO or CT efficacy and tumor burden a case control study

- Case-control patients, n=91
  - 144 NSCLC patients treated with IO
  - 413 historic controls treated without IO
  - Matched for stage, PS, histology, driver mutation, smoking status, initial treatment (CT vs CT-RT)
- Tumor size was analyzed using RECIST 1.1 criteria
- Benefit of IO restricted to small tumors**

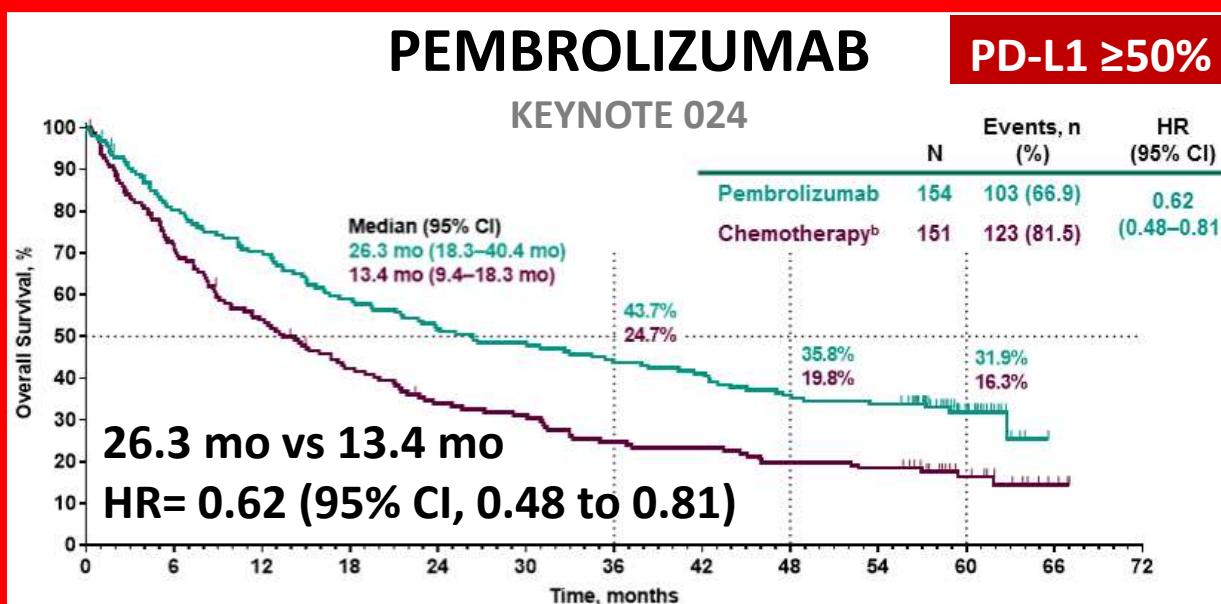


# PD-L1 $\geq$ 50% or high : First-Line single agent IO

## PEMBROLIZUMAB

KEYNOTE 024

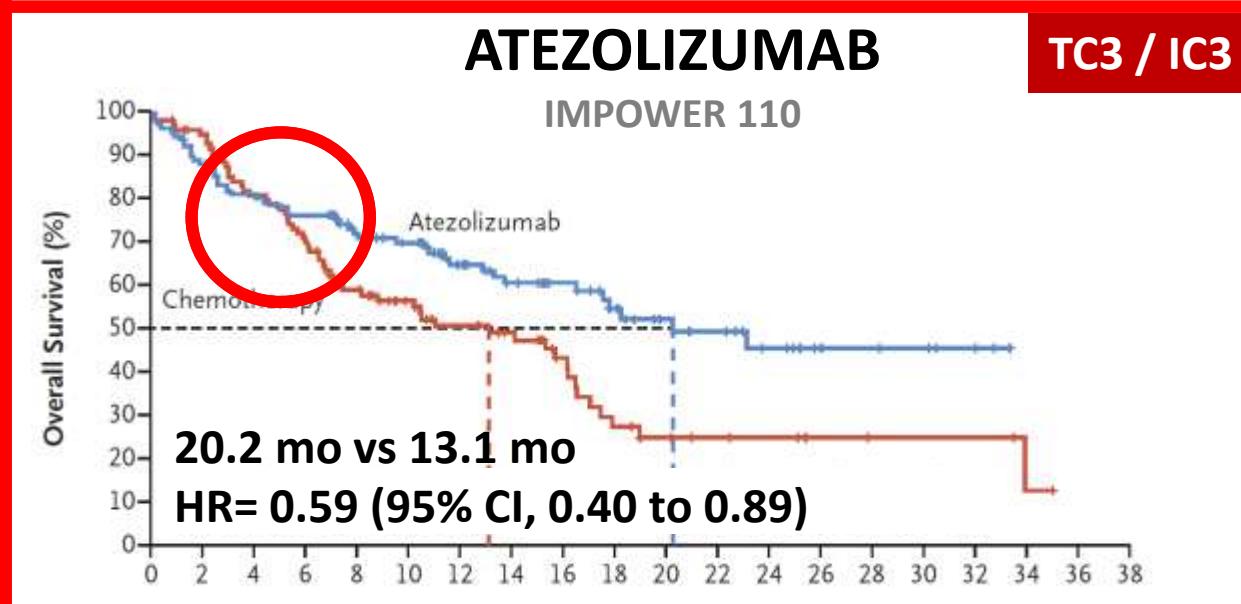
PD-L1  $\geq$ 50%



## ATEZOLIZUMAB

IMPOWER 110

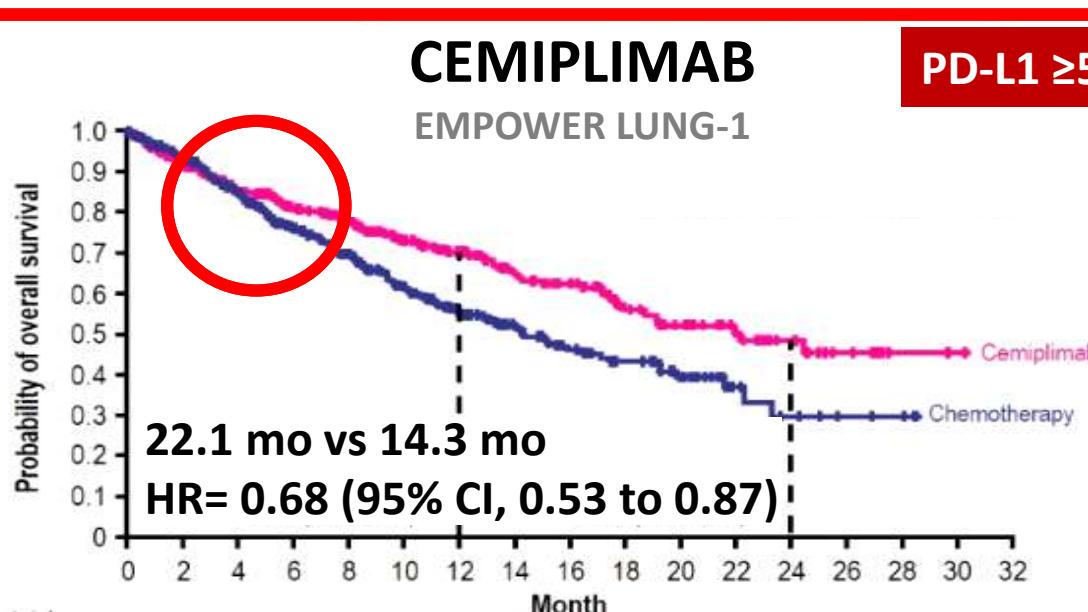
TC3 / IC3



## CEMIPPLIMAB

EMPOWER LUNG-1

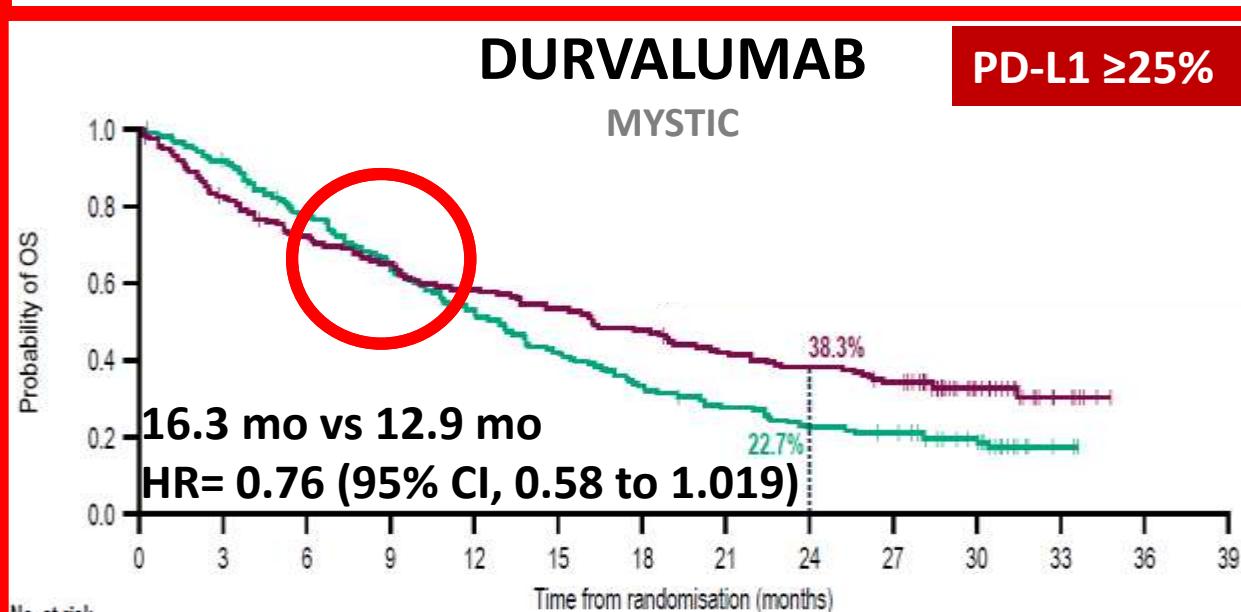
PD-L1  $\geq$ 50%



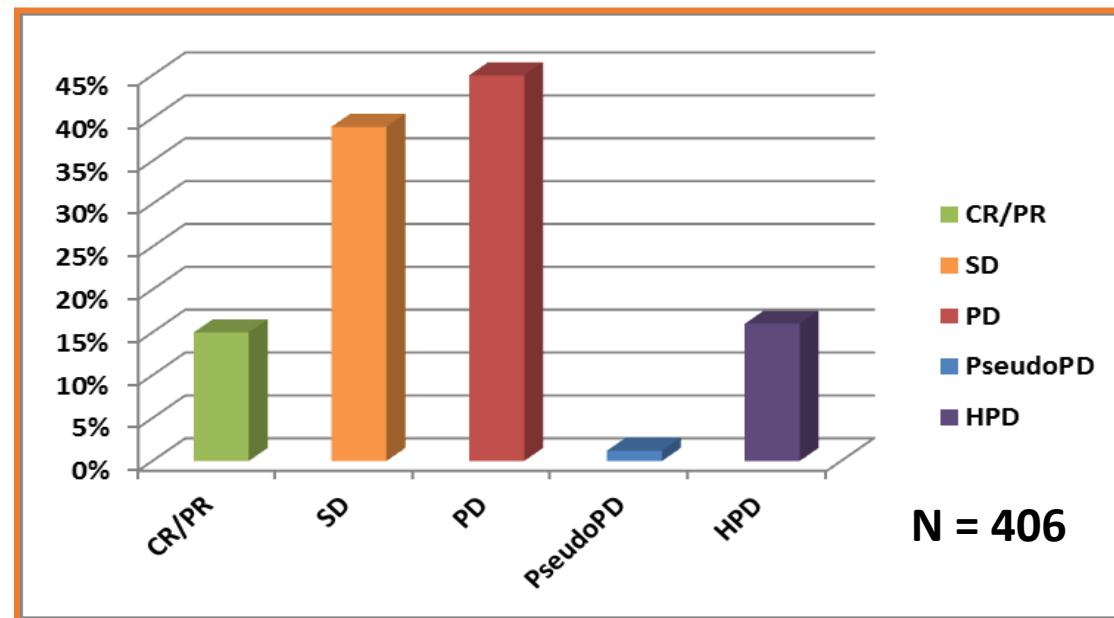
## DURVALUMAB

MYSTIC

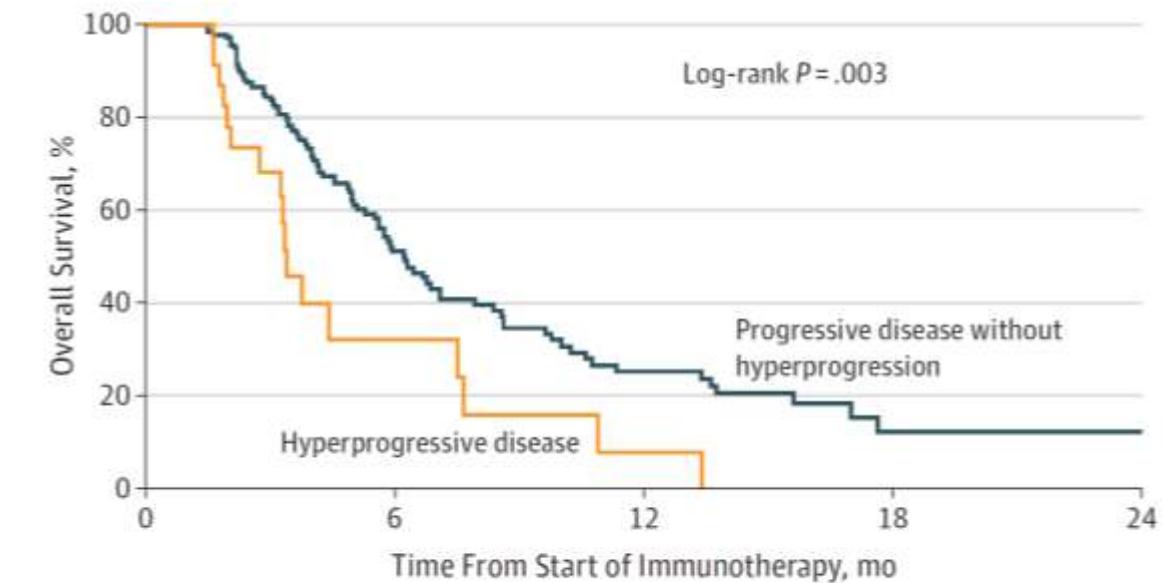
PD-L1  $\geq$ 25%



# Hyperprogressive disease



Hyperprogression : 13,8%

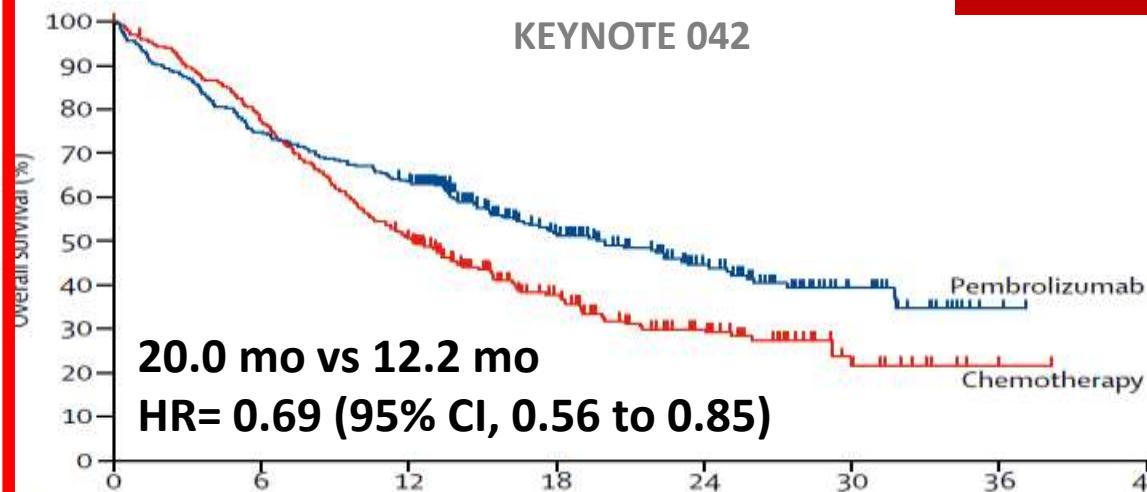


# PD-L1 $\geq$ 50% or high : IO vs CT-IO vs IO-IO

## PEMBROLIZUMAB

KEYNOTE 042

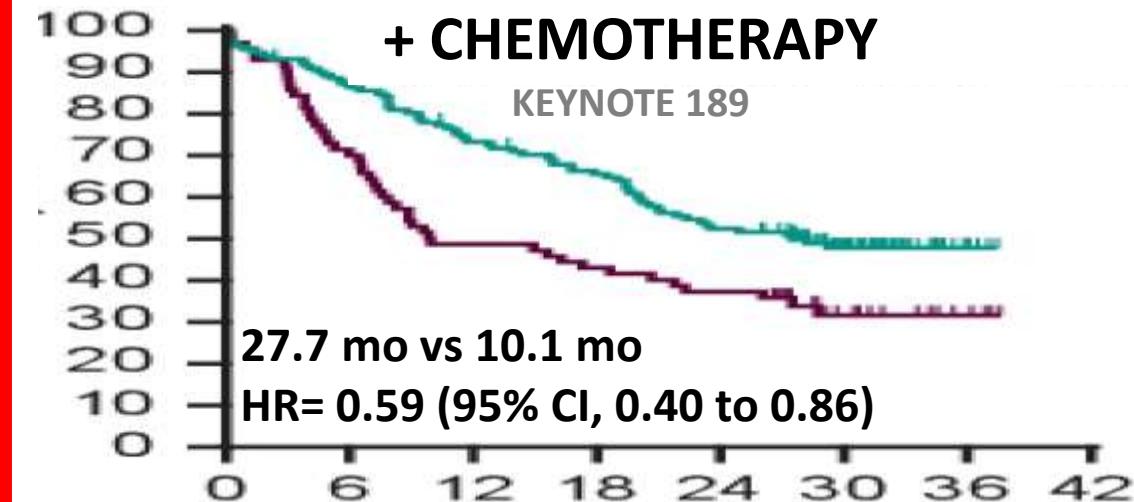
PD-L1  $\geq$ 50%



## PEMBROLIZUMAB + CHEMOTHERAPY

KEYNOTE 189

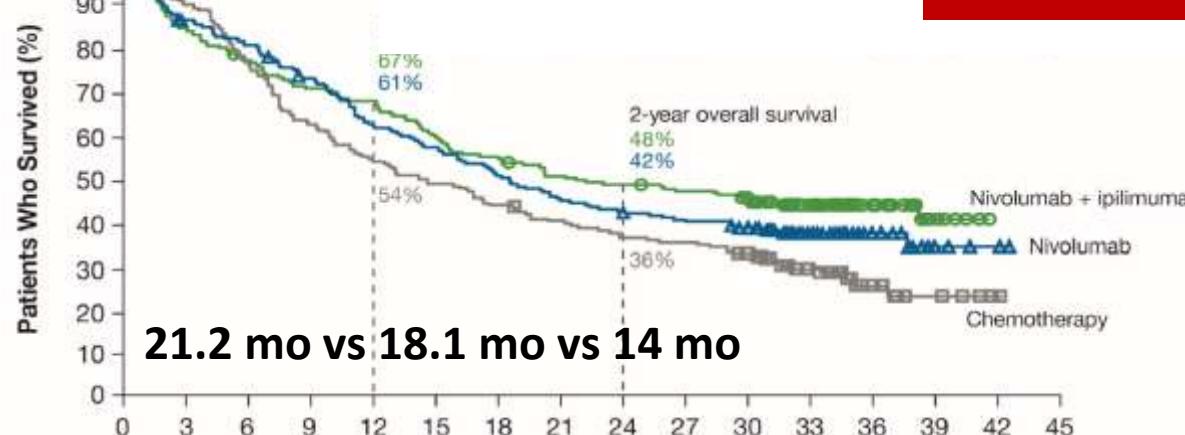
PD-L1  $\geq$ 50%



## IPILIMUMAB-NIVOLUMAB

CHECKMATE 226

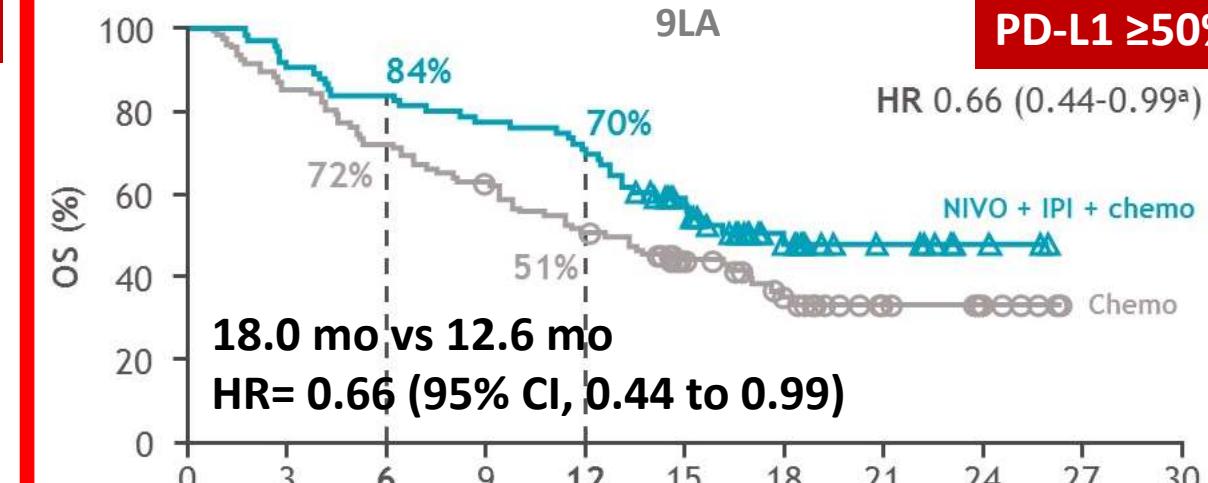
PD-L1  $\geq$ 50%



## CT + IPILIMUMAB-NIVOLUMAB

9LA

PD-L1  $\geq$ 50%

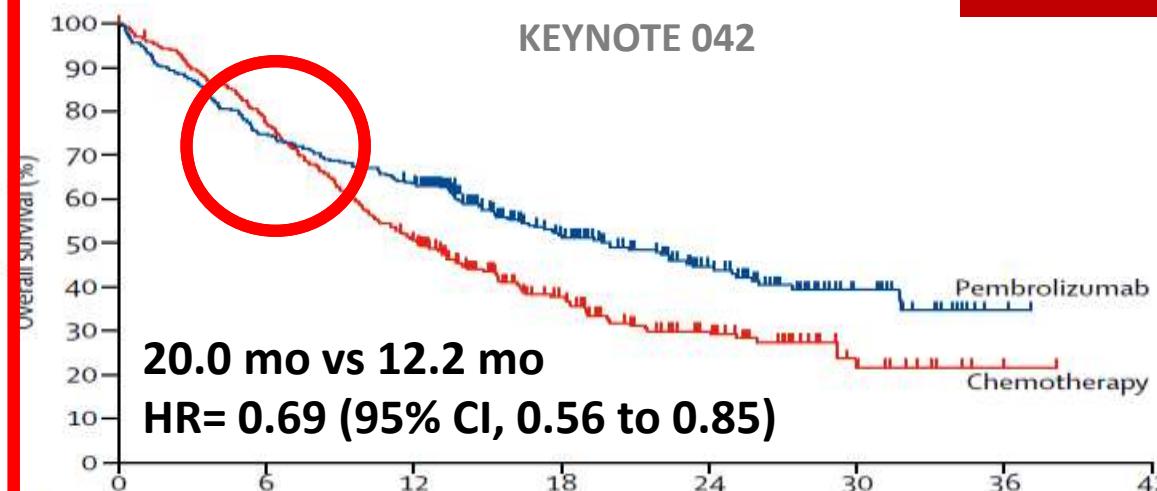


# PD-L1 $\geq$ 50% or high : IO vs CT-IO vs IO-IO

## PEMBROLIZUMAB

KEYNOTE 042

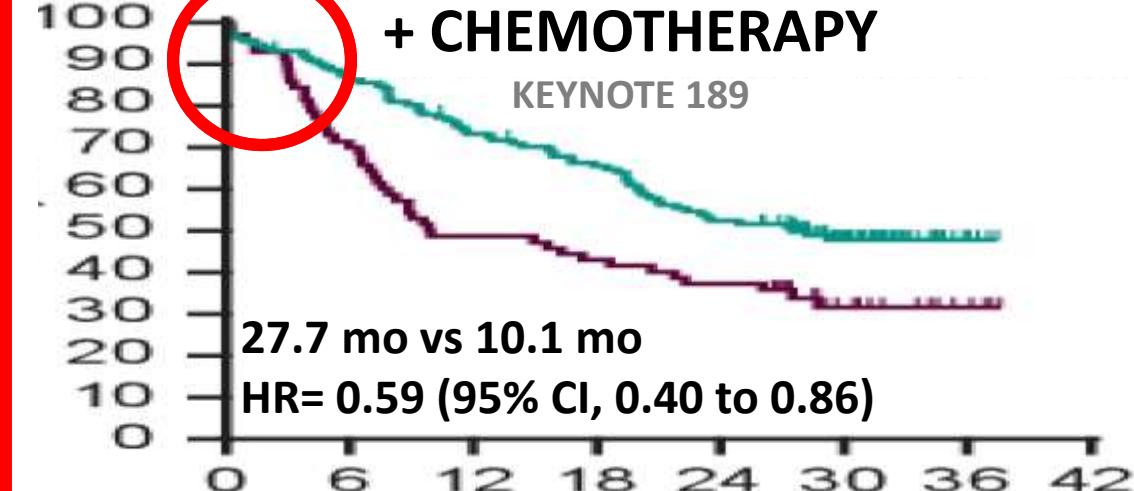
PD-L1  $\geq$ 50%



## PEMBROLIZUMAB + CHEMOTHERAPY

KEYNOTE 189

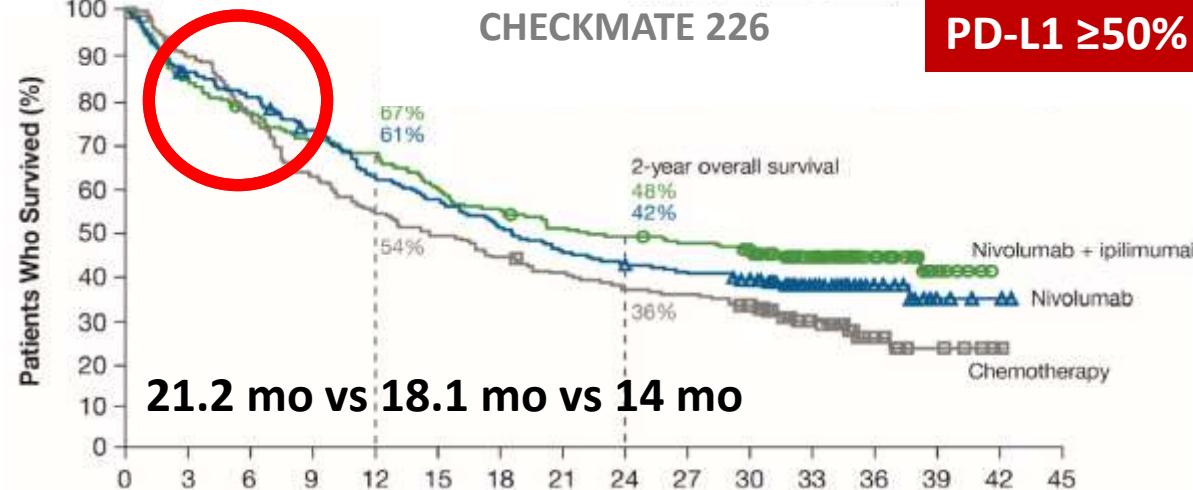
PD-L1  $\geq$ 50%



## IPILIMUMAB-NIVOLUMAB

CHECKMATE 226

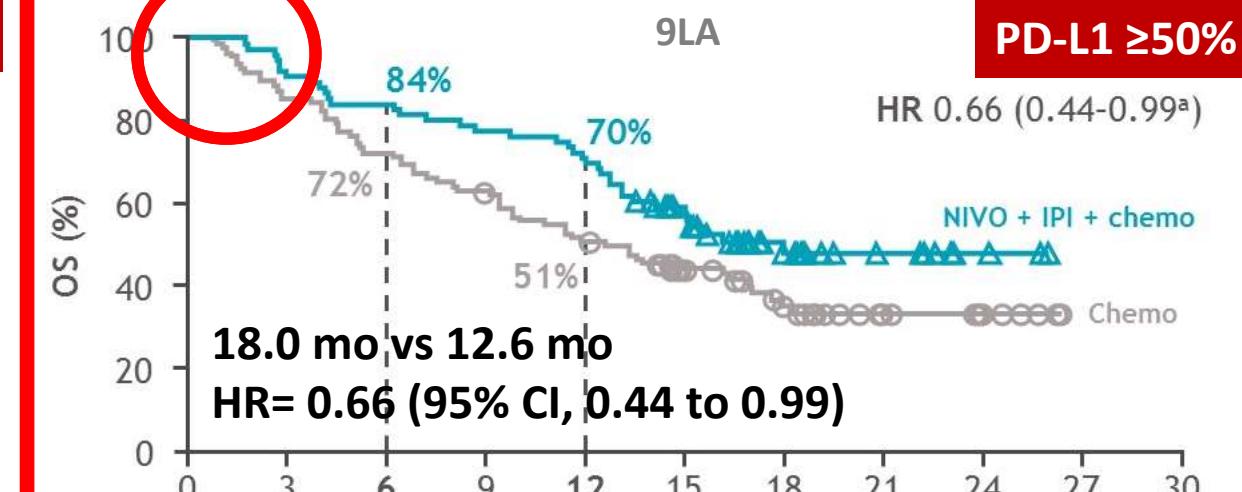
PD-L1  $\geq$ 50%



## CT + IPILIMUMAB-NIVOLUMAB

9LA

PD-L1  $\geq$ 50%



# Chemo-IO, IO-IO, or IO-mono

## Conclusion 1

- PD-L1  $\geq 50\%$ 
  - IO is a good option for selected patients (low tumor burden...)
  - IO-IO does not appear to be better than IO
  - CT-IO might be a better option for aggressive disease
  - CT-IO-IO does not appear to be better than CT-IO

# PD-L1 IHC

## *Is still the king*



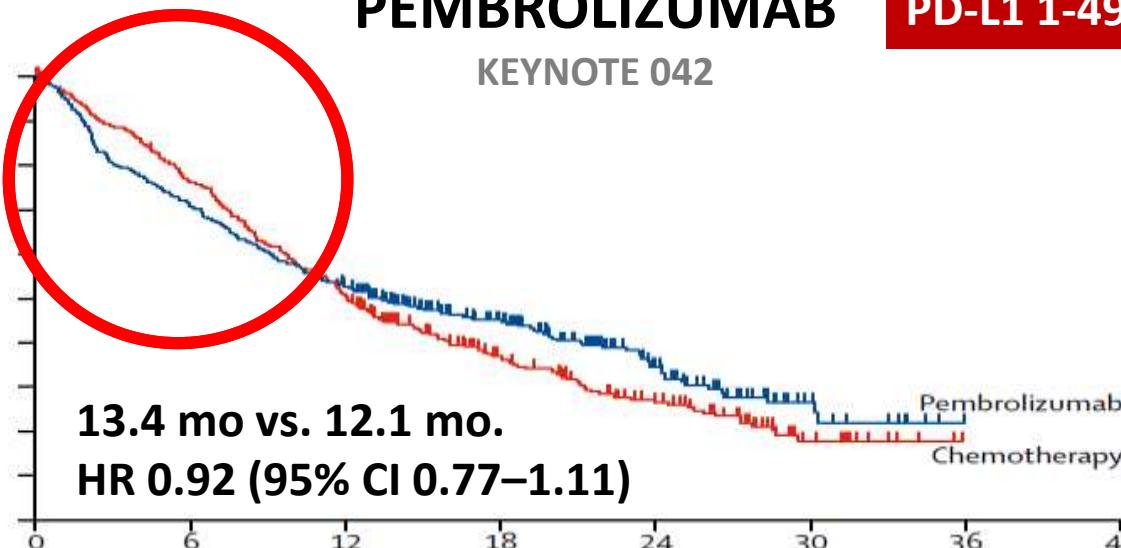
**PD-L1 1-49%**

# PD-L1 1-49% : IO vs CT-IO

## PEMBROLIZUMAB

KEYNOTE 042

PD-L1 1-49%

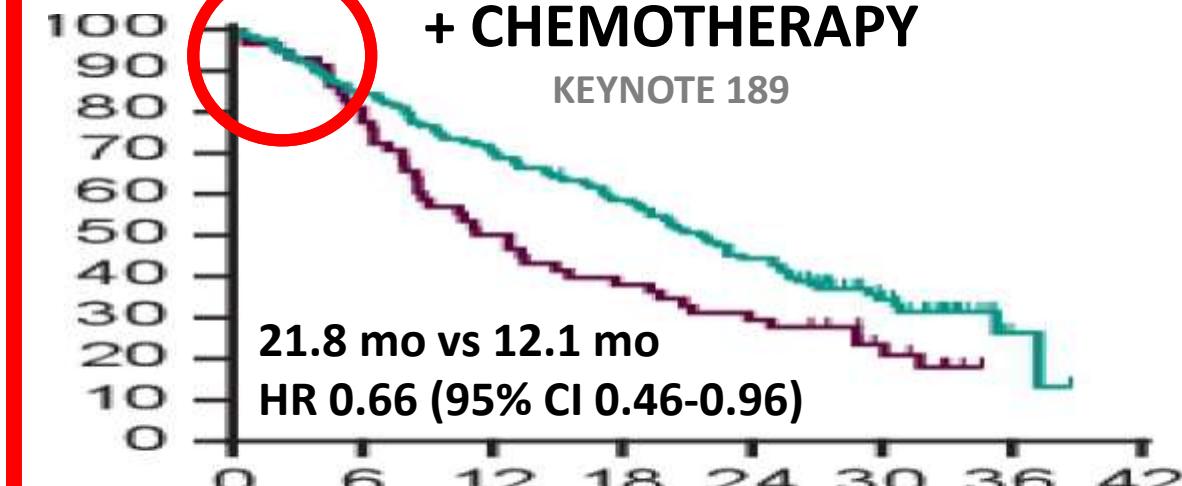


## PEMBROLIZUMAB

+ CHEMOTHERAPY

KEYNOTE 189

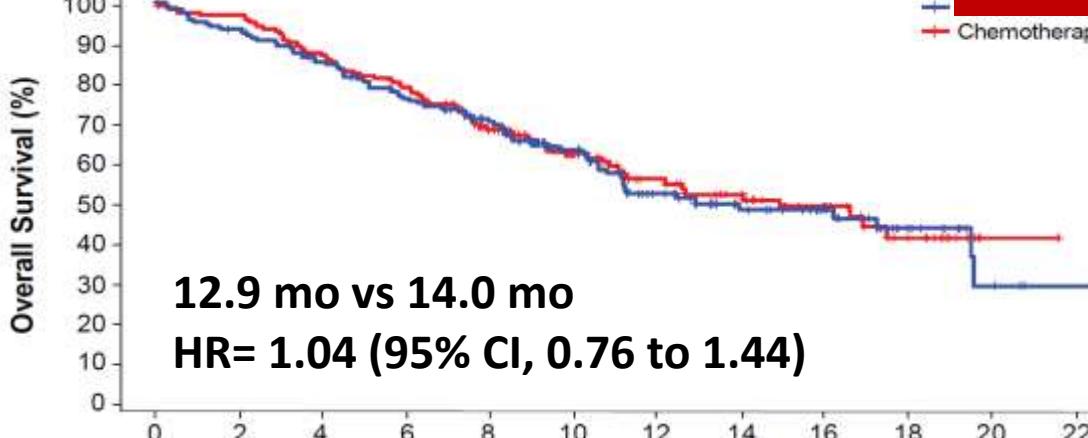
PD-L1 1-49%



## ATEZOLIZUMAB

IMPOWER 110

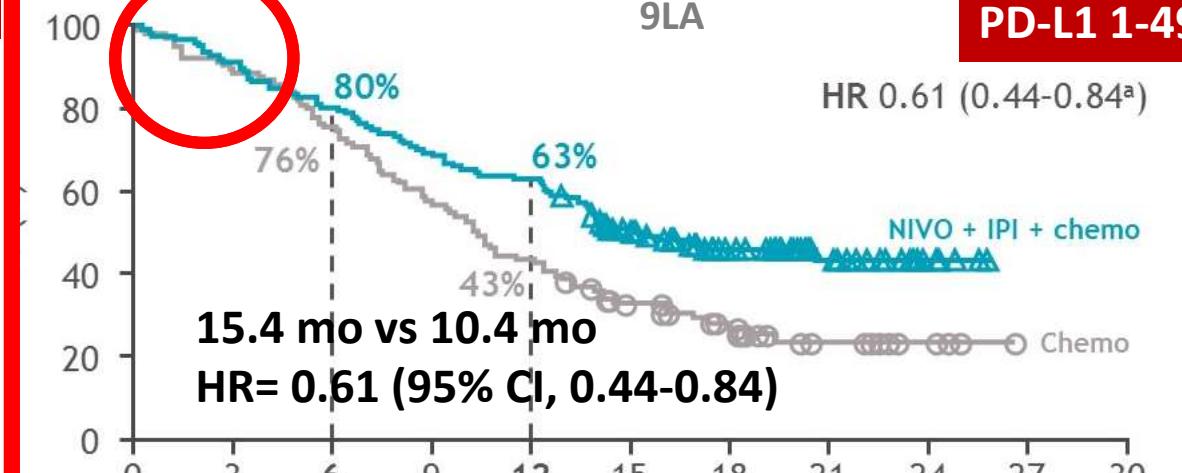
TC 1-2  
IC 1-2-WT



## CT + IPILOMUMAB-NIVOLUMAB

9LA

PD-L1 1-49%

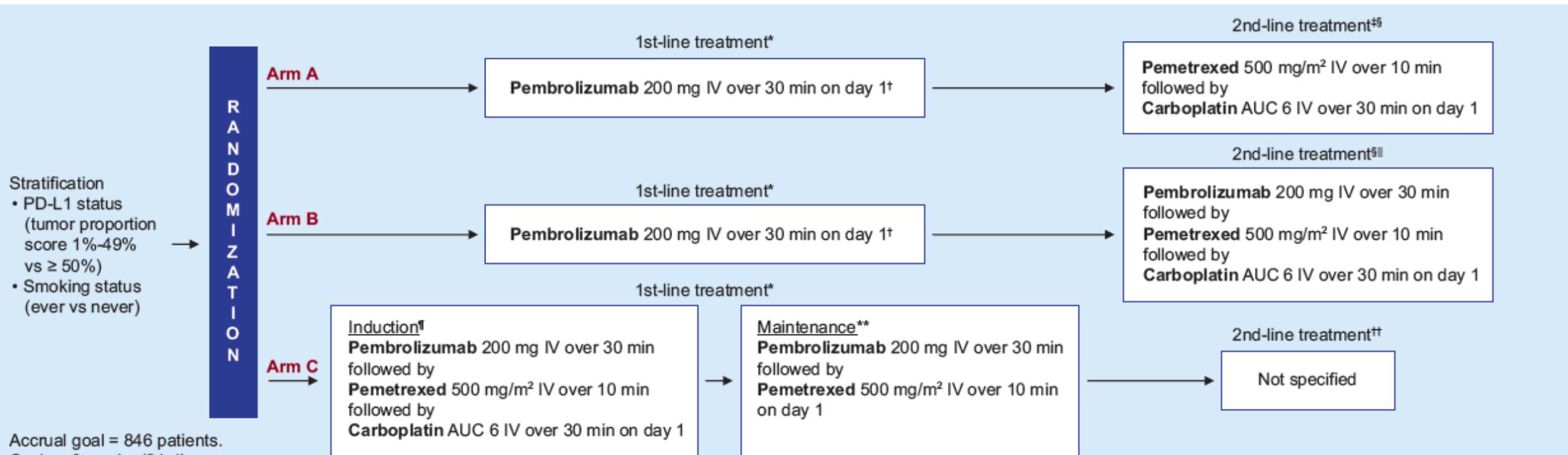


# Chemo-IO, IO-IO, or IO-mono

## Conclusion 2

- PD-L1 1-49%
  - Single IO is a poor option
  - IO-IO does not appear to be better than IO
  - CT-IO is the standard of care
  - CT-IO-IO does not seem to be better than CT-IO

# INSIGNA trial ongoing



\*Repeat until progression or maximum of 2 years. If patient does not progress onto 2nd-line treatment, proceed to long-term follow-up. If maximum treatment duration is reached prior to progression, or treatment is discontinued for any reason, patient remains in observation until progression.

<sup>†</sup>If no progression by 2 years of pembrolizumab (MK-3475), patient continues on observation until progression, at which time proceed to 2nd-line therapy within 6 weeks of progression.

<sup>‡</sup>Repeat for 4 cycles or until disease progression. Pemetrexed can then be given as maintenance until disease progression per standard of care.

<sup>§</sup>Following completion of 2nd-line treatment, patient will proceed to long-term follow-up.

<sup>||</sup>Repeat for 4 cycles or until disease progression. Pembrolizumab and pemetrexed can then be given as maintenance until disease progression or 2 years of pembrolizumab treatment in total.

Pemetrexed alone may continue per standard of care.

<sup>¶</sup>Repeat for 4 cycles, then proceed to maintenance. If disease progression occurs prior to the completion of 4 cycles, patient should instead enter long-term follow-up and continue to the 2nd-line treatment off study, per standard of care.

<sup>\*\*</sup>Repeat for 2 years of total treatment across induction and maintenance, or until disease progression. If after 2 years there is no progression, pemetrexed alone may continue per standard of care.

<sup>††</sup>Patient enters long-term follow-up and receives 2nd-line treatment off study, per standard of care.

PD-L1 = programmed death-ligand 1.

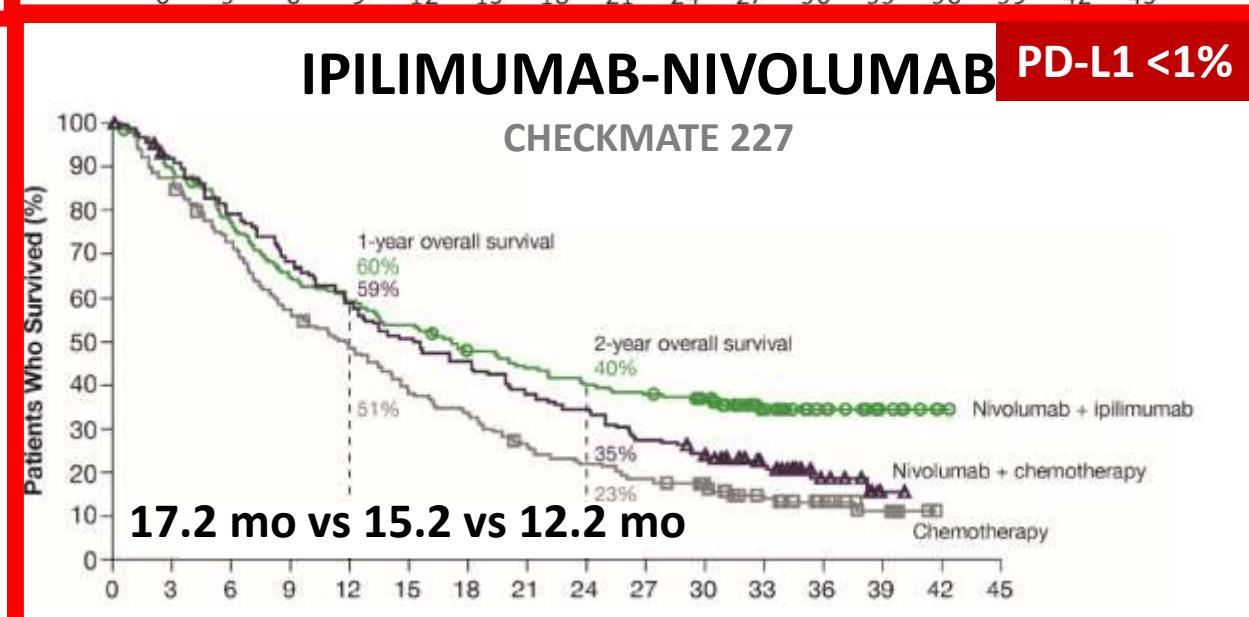
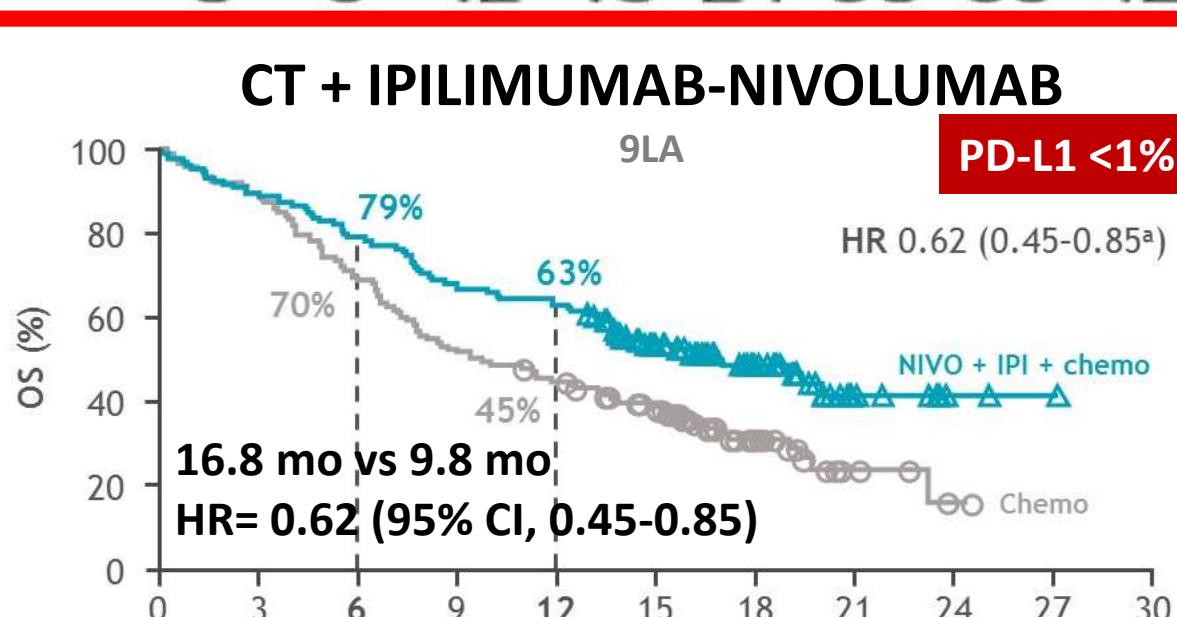
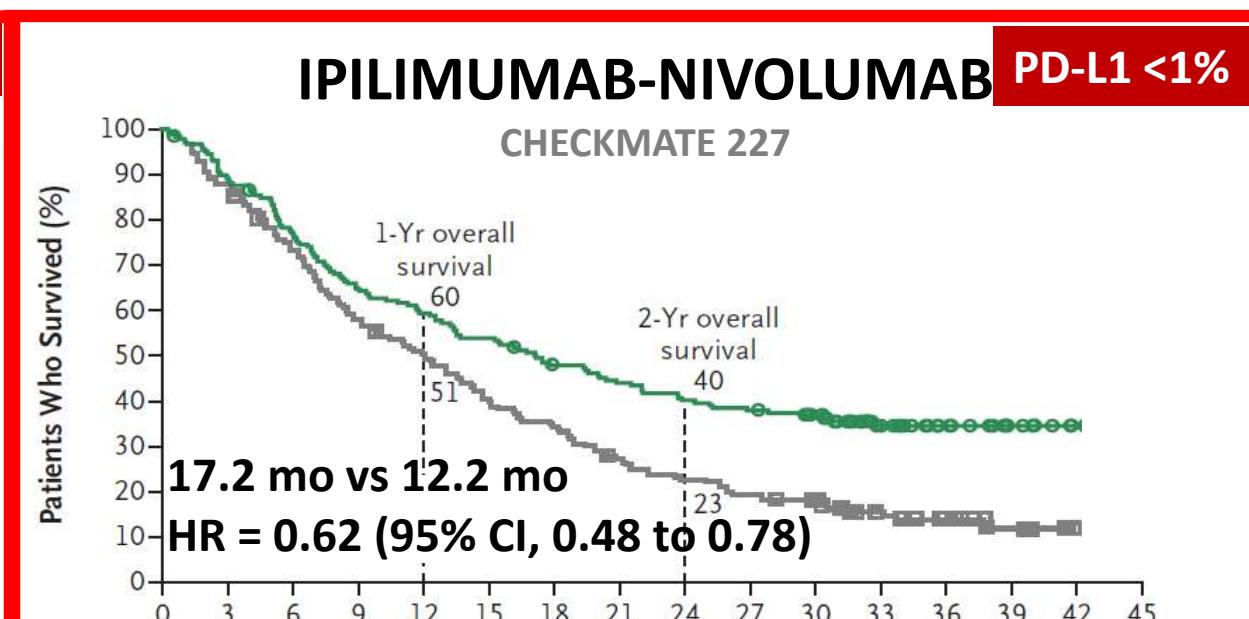
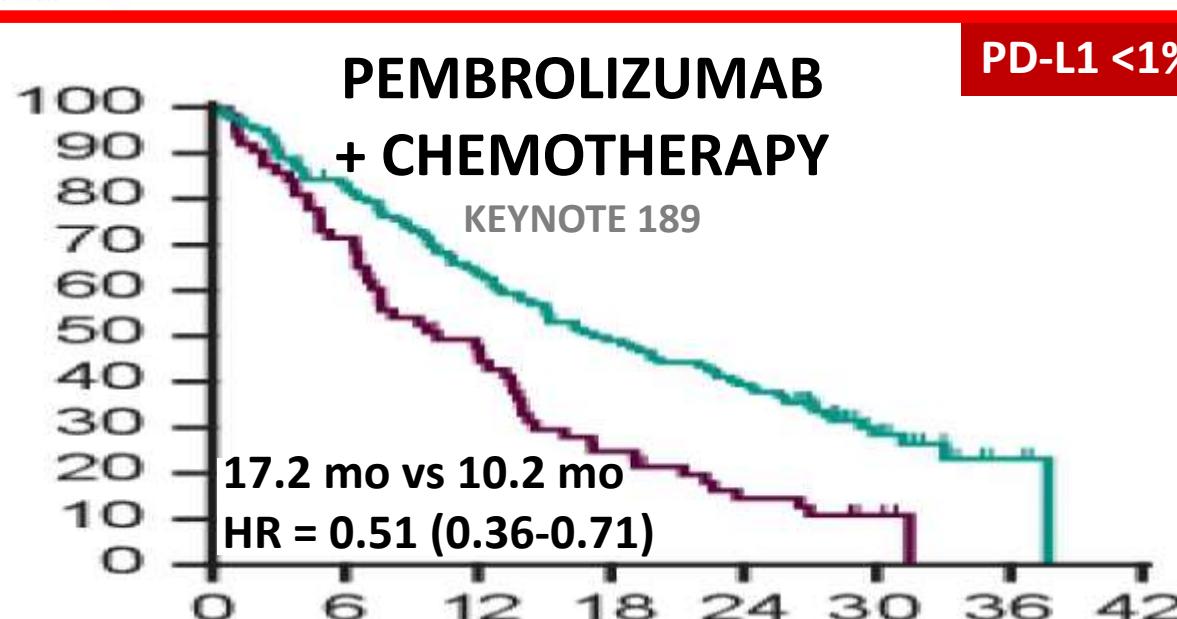
# PD-L1 IHC

## *Is still the king*



**PD-L1 <1%**

# PD-L1<1% CT-IO vs IO-IO

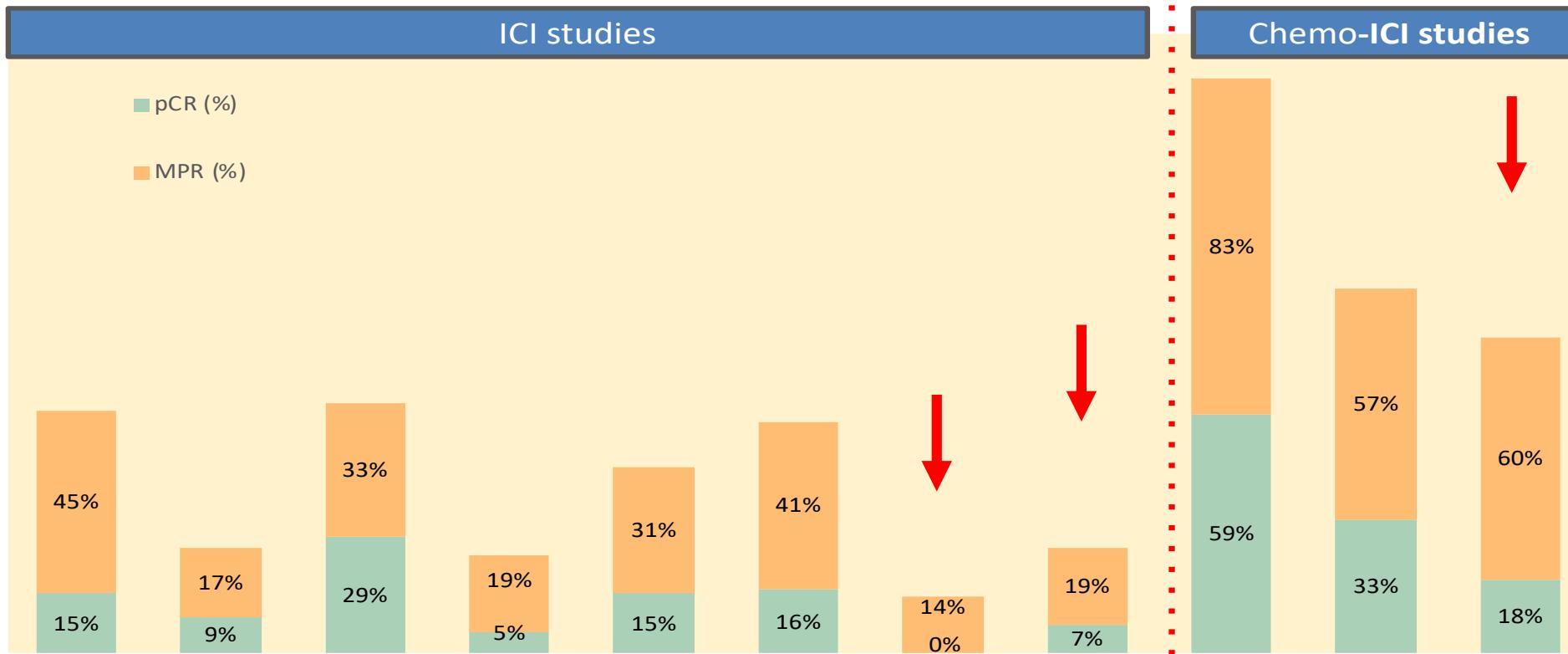


# Chemo-IO, IO-IO, or IO-mono

## Conclusion 3

- PD-L1 <1%
  - Single IO is NOT an option
  - (CT)-IO-IO has interesting preliminary data
  - CT-IO is the standard of care

# Neoadjuvant IO



	Forde et al.	NEOSTAR	LCMC3	MK3475-223	Li et al.	PRINCEPS	IONESCO	NADIM	COLUMBIA	SAKK 16/14
N	22	23	21	101	15	40	30	50	46	67
Stage	I-IIIA	I-IIIA	I-IIIA	IB-IIIA	I-II	IB-IIIA	I-IIIA	IB-IIIA	IIIA	IIIA (N2)
Surgery	95%	96%	81%	89%	87%	93%	100%	92%	90%	82%
RR	10%	22%	19%	7%	NR	20%	7%	9%	74	58%

Neoadjuvant ICI trials in early-stage NSCLC

Benitez et al. Clinical Cancer Research 2020

# SCREEN!

*A special thanks to*



Jordi Remon



Laura Mezquita



Jose Benitez



David Planchard