Traitement de première ligne des CBNPCs sans addiction oncogénique

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Disclosure

- Clinical research:
- Amgen
- Astra-Zeneca
- Abbvie
- Blue
- BMS
- Boehringer-Ingelheim
- Janssen
- Hoffmann-La Roche
- Lilly
- Merck
- MSD
- Novartis
- Sivan
- Trizell

- Symposia:
- Amgen
- Astra-Zeneca
- BMS
- Janssen
- Mirati
- MSD
- Pfizer

- Hospitality:
- Astra-Zeneca
- MSD

- ITMIG: President

- Consultancy:
- Amgen
- Astra-Zeneca
- BMS
- Boehringer-Ingelheim
- Janssen
- Hoffman-La Roche
- Lilly
- Novartis
- Merck
- MSD
- Pfizer
- Sanofi

Public disclosure
https://dpi.sante.gouv.fr/dpi-public-webapp/app/recherche/declarant

Les cancers thoraciques

Non à petites cellules

- Stades précoces
- Dépistage
- Localement avancés
  - Résécables
  - Non résécables
- Métastatiques
  - Oncogène addictif
  - Sans oncogène addictif

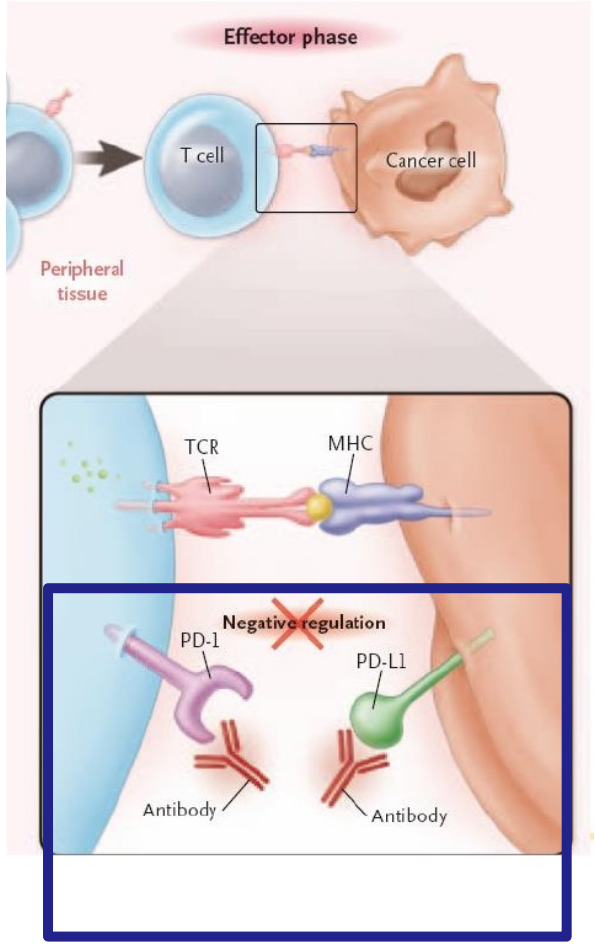
Petites cellules

- Localement avancés
- Métastatiques

Mésothéliome

Tumeurs thymiques

PD-1/PD-L1 checkpoint inhbitors



Target	Antibody	Type	Company
PD-1	Nivolumab	Humanised IgG4	BMS
	Pembrolizumab	Humanised IgG4	MSD
	Cemiplimab	Humanised IgG4	Sanofi
	Sintilimab	Humanised IgG4	Lilly
	Camrelizumab	Humanised IgG4	Jiangsu Hengrui
	Tislelizumab	Humanised IgG4	Beigene, Novartis
	Toripalimab	Humanised IgG4	Coherus
PD-L1	Durvalumab	IgG1	MedImmune/Astra-Zeneca
	Atezolizumab	IgG1	Genentech/Roche
	Sugemalimab	IgG1	Cstone

Ribas. N Engl J Med 2012; 366:2517

#1 Immunotherapy to replace chemotherapy

Immunotherapy to replace chemotherapy

Immunotherapy in addition to chemotherapy

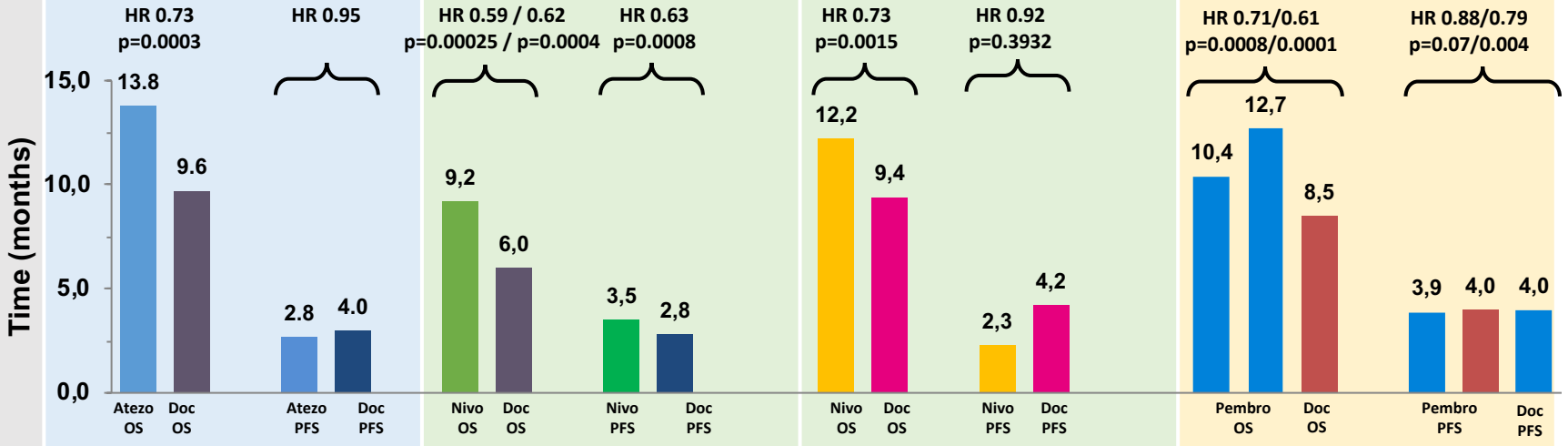
Immunotherapy *after* chemoradiotherapy

#1 Immunotherapy to replace chemotherapy

Second line
vs.
Docetaxel

#1 Immunotherapy to replace chemotherapy

Second line vs. Docetaxel

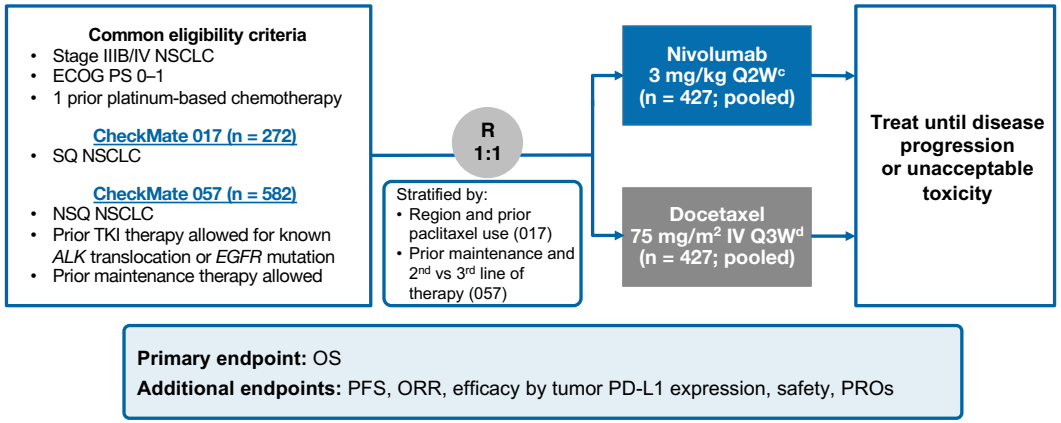
	Atezolizumab	Nivolumab		Pembrolizumab
	OAK PhIII allcomer 2/3L atezo vs. doc (n=850)	CheckMate 017 PhIII 2L Sq nivo vs. doc (n=272)	CheckMate 057 PhIII 2/3L NSq nivo vs. doc (n=582)	KEYNOTE-010 PhIII PDL1+ ≥2L pembro vs. doc (n=1034)
				
OR %	**Atezo 14% vs doc 13%**	**Nivo 20% vs doc 9%**	**Nivo 19% vs doc 12%**	**Pembro 18% vs doc 9%**
Notes	G3–4 treatment-related AEs: 15 vs 43%	G3–4 treatment-related AEs: 8 vs 56% *Reduction from baseline in lung cancer symptoms with nivolumab*	G3–4 treatment-related AEs: 10 vs 54%	G3–5 treatment-related AEs: 13-16 vs 35%
	ALL histologies ALL PD-L1	**2 trials for 2 histologies ALL PD-L1**		**ALL histologies PD-L1≥1%**

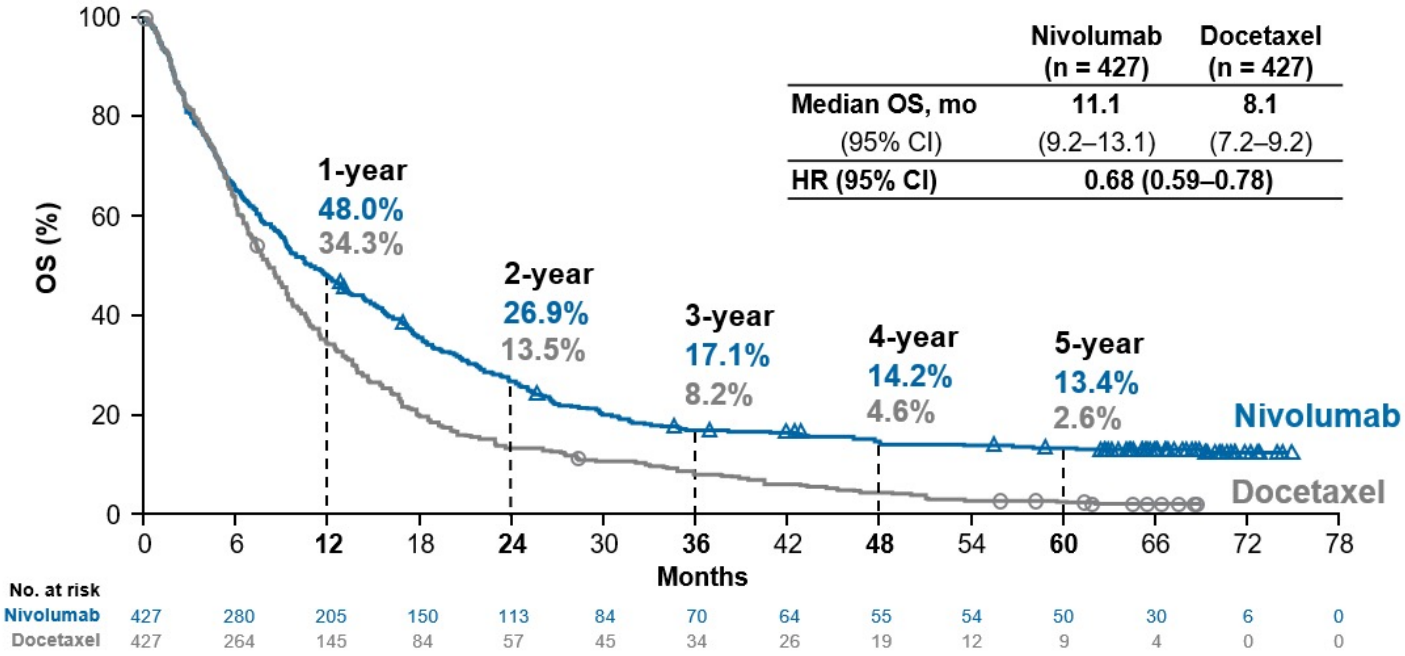
Cross-study comparisons are not intended.

Felip E et al. J Clin Oncol 2017;
Herbst RS et al.
Rittmeyer A et al. *Lancet.* 2017;389:255

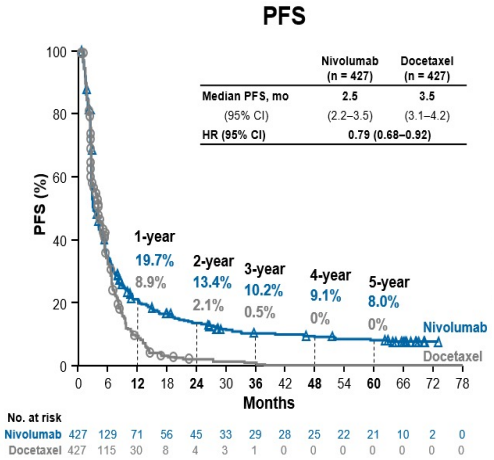
Immune checkpoint inhibitors
Prolonged survival in responders: 5-year OS is reachable

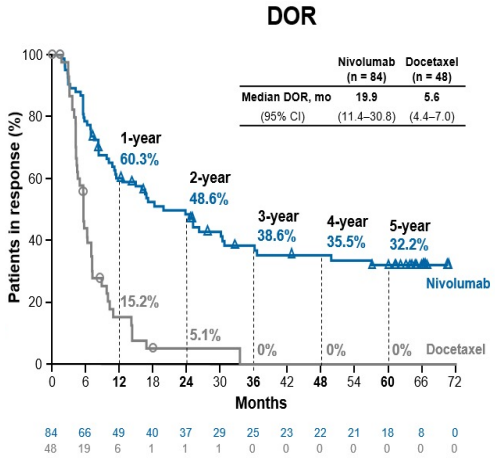
CHECKMATE-017/-057

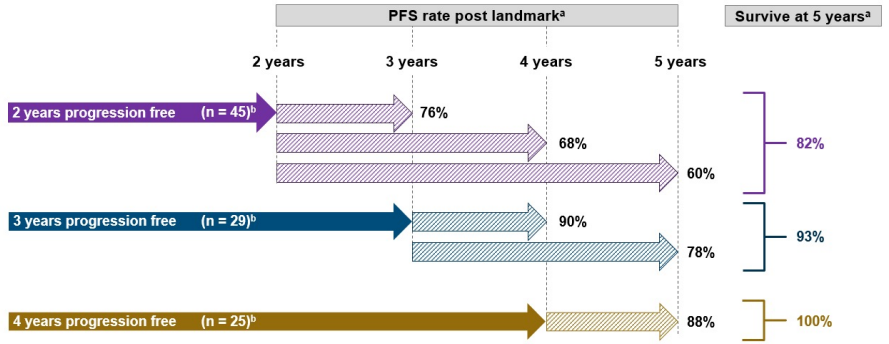




	Nivolumab (n = 427)	Docetaxel (n = 427)
Median OS, mo	11.1	8.1
(95% CI)	(9.2–13.1)	(7.2–9.2)
HR (95% CI)	0.68 (0.59–0.78)	



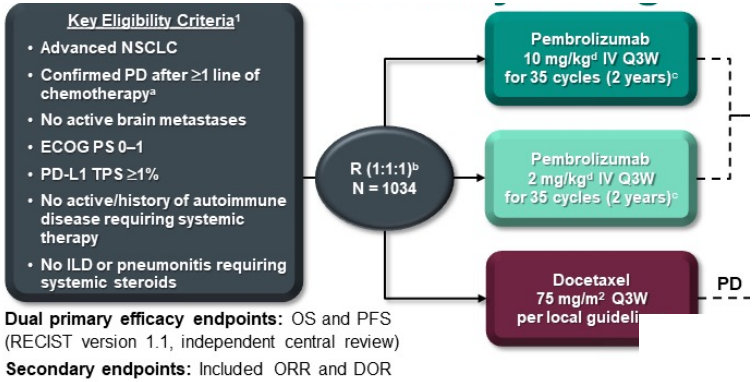




Gettinger et al. WCLC 2019

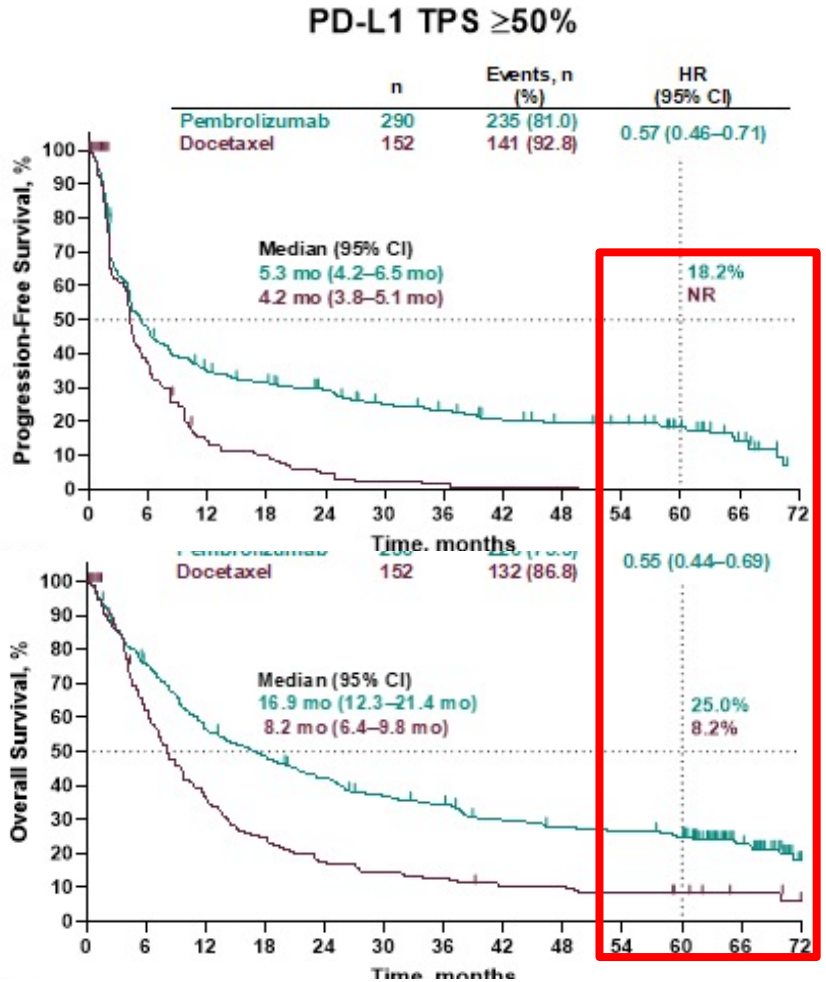
Immune checkpoint inhibitors
Prolonged survival in responders: 5-year OS is reachable

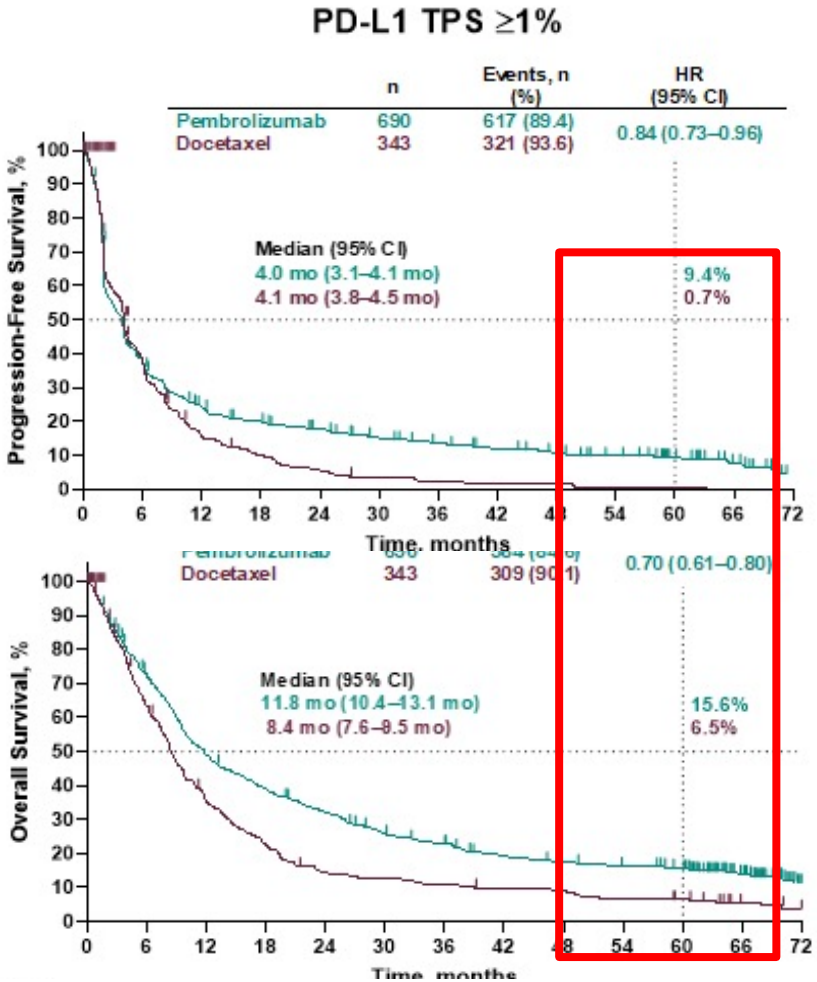
KEYNOTE-010: Pembrolizumab



Dual primary efficacy endpoints: OS and PFS (RECIST version 1.1, independent central review)

Secondary endpoints: Included ORR and DOR





Herbst R et al. Abstr FP13.01 WCLC 2020

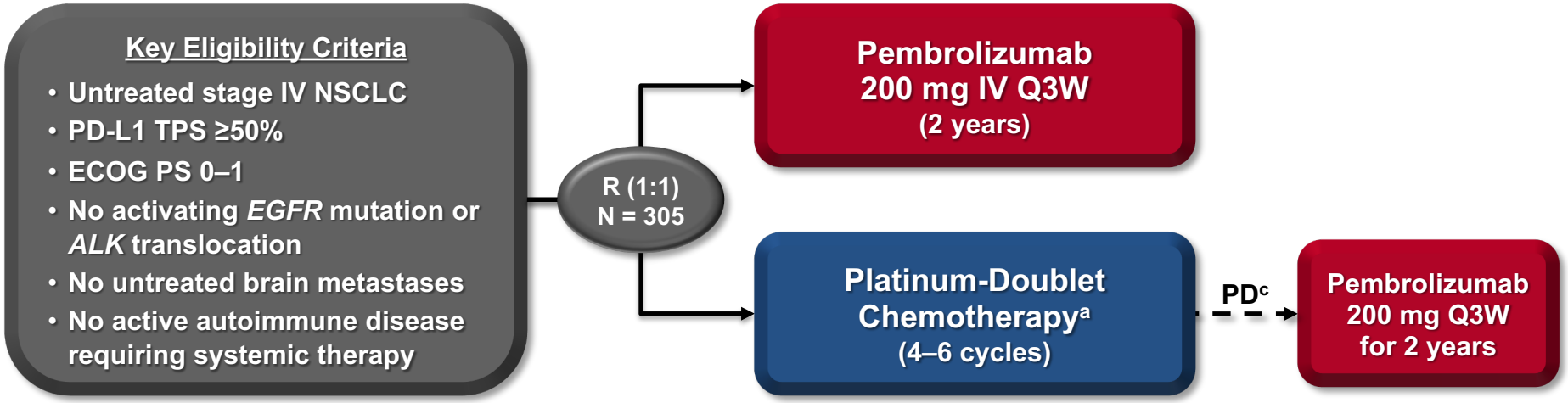
#1 Immunotherapy to replace chemotherapy

Second line
vs.
Docetaxel

First line
vs.
Platin-based doublet

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

KEYNOTE-024: design



End Points

Primary:	PFS (RECIST v1.1, blinded independent central review)
Key secondary:	OS
Secondary:	ORR, safety
Exploratory:	DOR

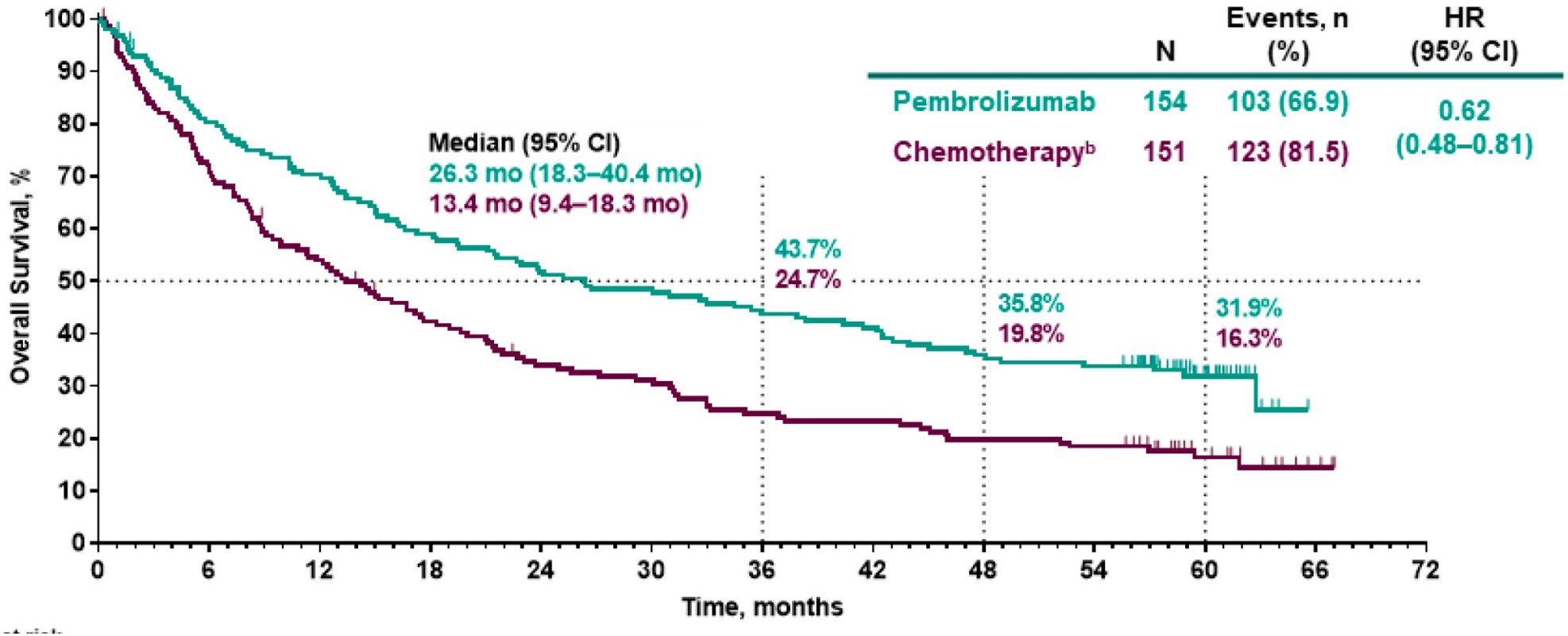
[a]Optional pemetrexed maintenance therapy for nonsquamous disease. [b]Permitted for nonsquamous disease only.
[c]Prior to the DMC recommendation and amendment 6, which permitted those in the chemotherapy arm to be offered pembrolizumab (based on interim analysis 2 data), patients were eligible for crossover when PD was confirmed by blinded, independent central radiology review.

Reck et al. N Engl J Med 2016; 375:1823

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

KEYNOTE-024: results

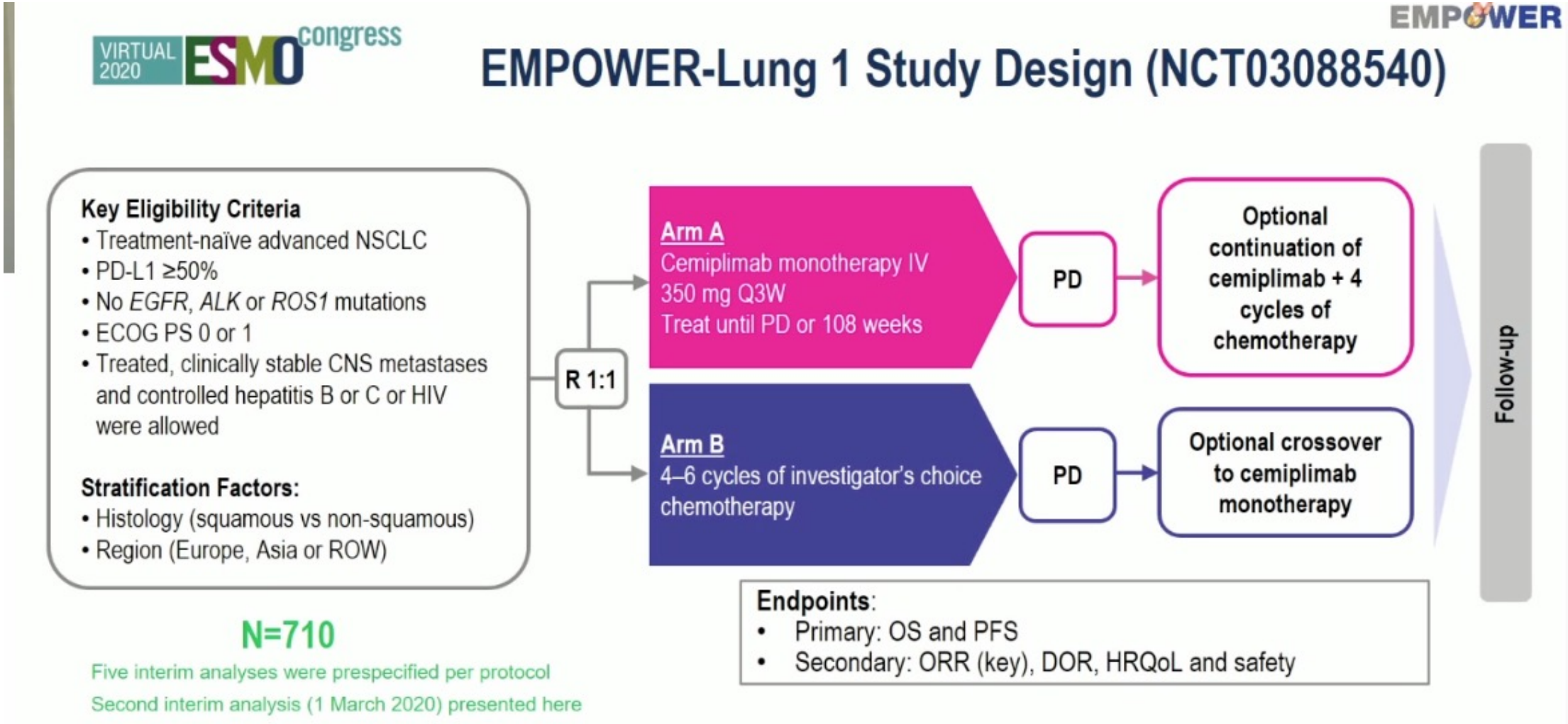
Overall Survival[a]



Brahmer et al. ESMO 2020

ESMO 2020: cemiplimab

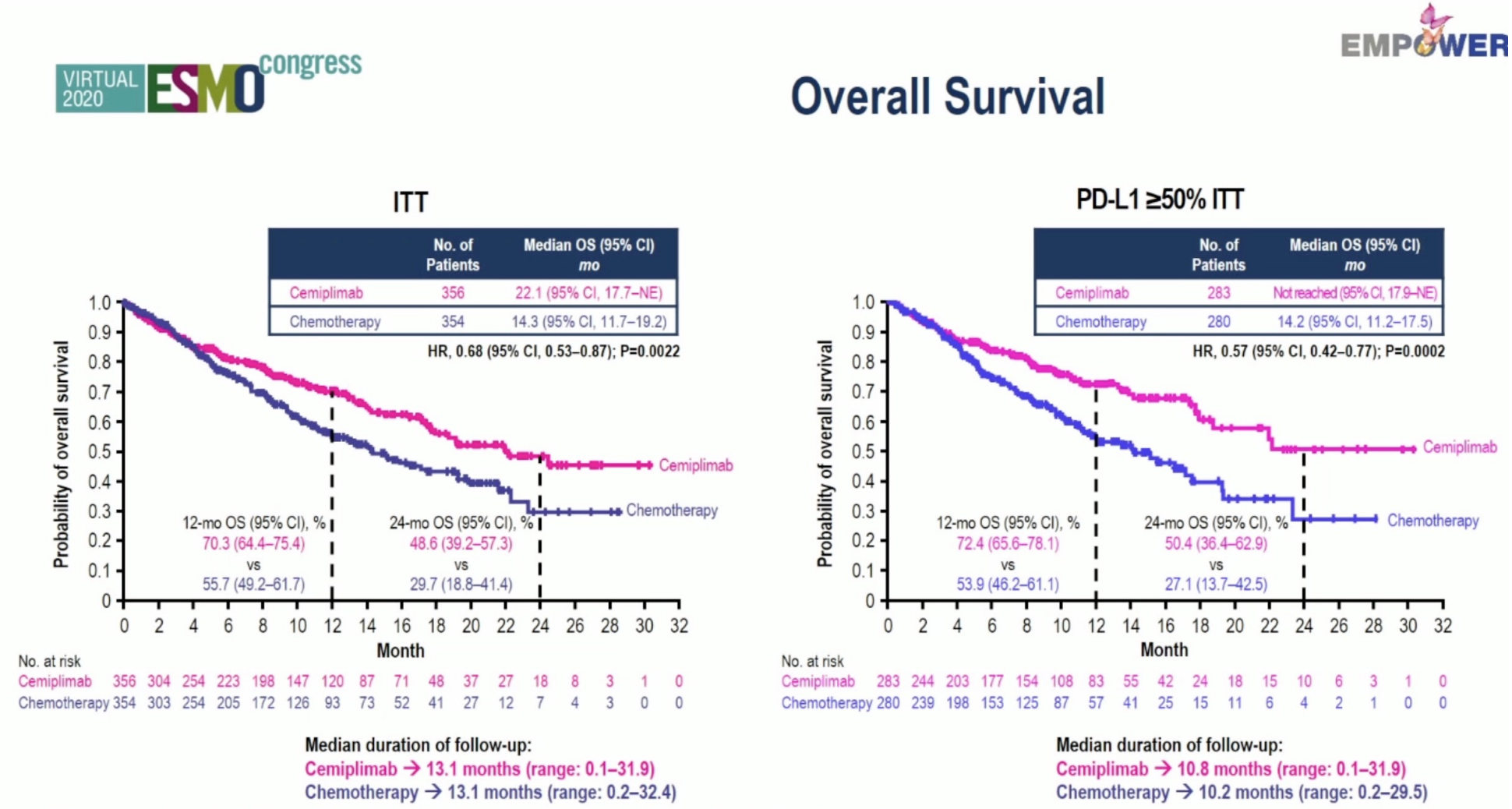
EMPOWER-Lung-1



Sezer et al. ESMO 2020

ESMO 2020: cemiplimab

EMPOWER-Lung-1



Sezer et al. ESMO 2020

#1 Immunotherapy to replace chemotherapy

Second line
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Selection on
PD-L1≥50%

Selection on
lower PD-L1?

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥1%

KEYNOTE-042 Study Design

Key Eligibility Criteria
- Untreated locally advanced or metastatic NSCLC of any histology
- PD-L1 TPS ≥1%[a]
- No sensitizing *EGFR* or *ALK* alterations
- ECOG PS 0 or 1
- No untreated or unstable CNS metastases
- No history of pneumonitis that required systemic corticosteroids

Stratification Factors
- Region (east Asia vs rest of the world)
- ECOG PS (0 vs 1)
- Histology (squamous vs nonsquamous)
- PD-L1 TPS (≥50% vs 1%–49%)

Randomize 1:1

N = 637 → Pembrolizumab 200 mg Q3W for up to 35 cycles

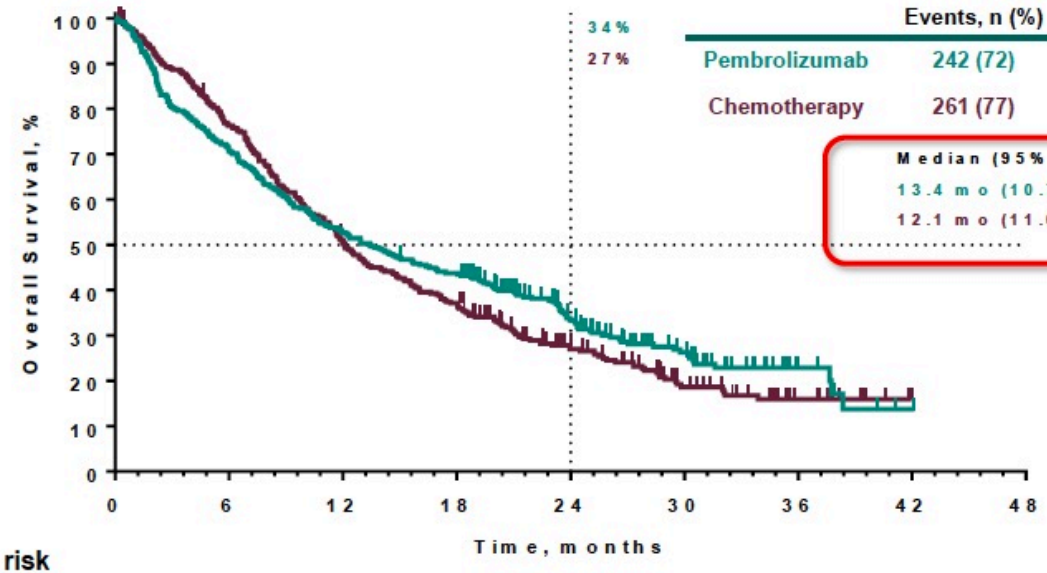
N = 637 → Carboplatin AUC 5 or 6 Q3W + Paclitaxel 200 mg/m² Q3W[b] OR Carboplatin AUC 5 or 6 Q3W + Pemetrexed 500 mg/m² Q3W[b] for up to 6 cycles

End points
- Primary: OS in PD-L1 TPS ≥50%, ≥20%, and ≥1%
- Secondary: PFS and ORR in TPS ≥50%, ≥20%, and ≥1%; safety in TPS ≥1%

Current analysis planned to occur ~45 months after study start

CNS, central nervous system.

Overall Survival: TPS 1%–49%[a]



	Events, n (%)	HR (95% CI)
Pembrolizumab	242 (72)	0.91 (0.77–1.09)
Chemotherapy	261 (77)	

Median (95% CI)
13.4 mo (10.7–16.9)
12.1 mo (11.0–14.0)

No. at risk									
Pembro/Pem/Plat	338	239	178	147	84	41	9	0	0
Placebo/Pem/Plat	337	254	168	123	67	34	12	0	0

Mok et al. ELCC 2019

#1 Immunotherapy to replace chemotherapy

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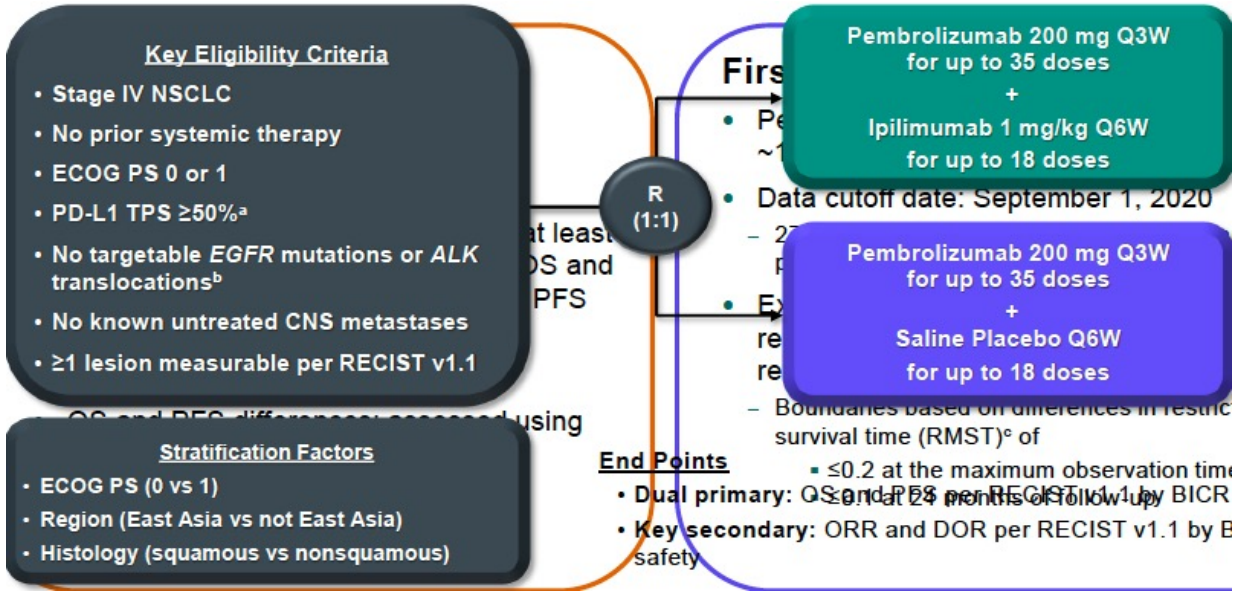
Selection on
PD-L1≥50%

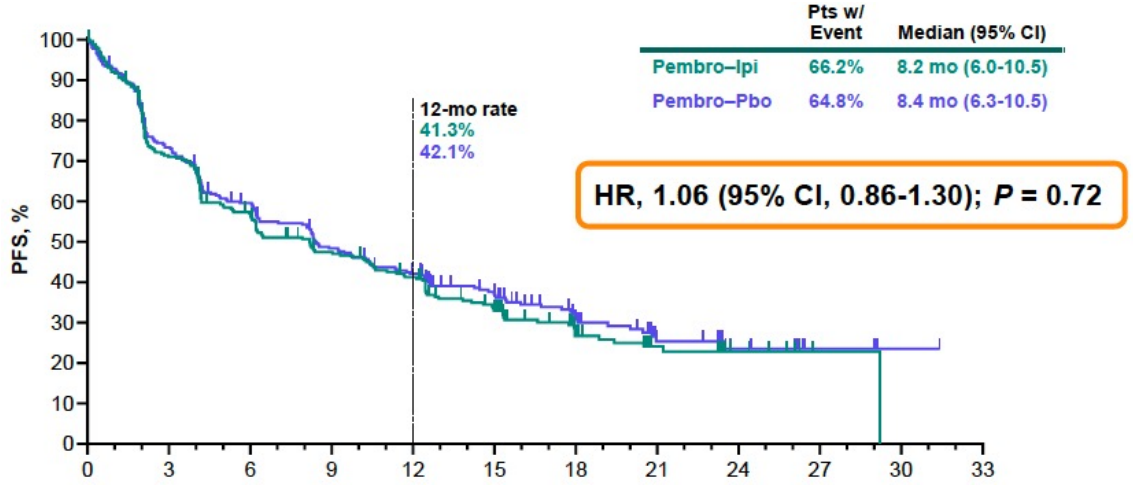
Selection on
lower PD-L1?

How to
optimise?

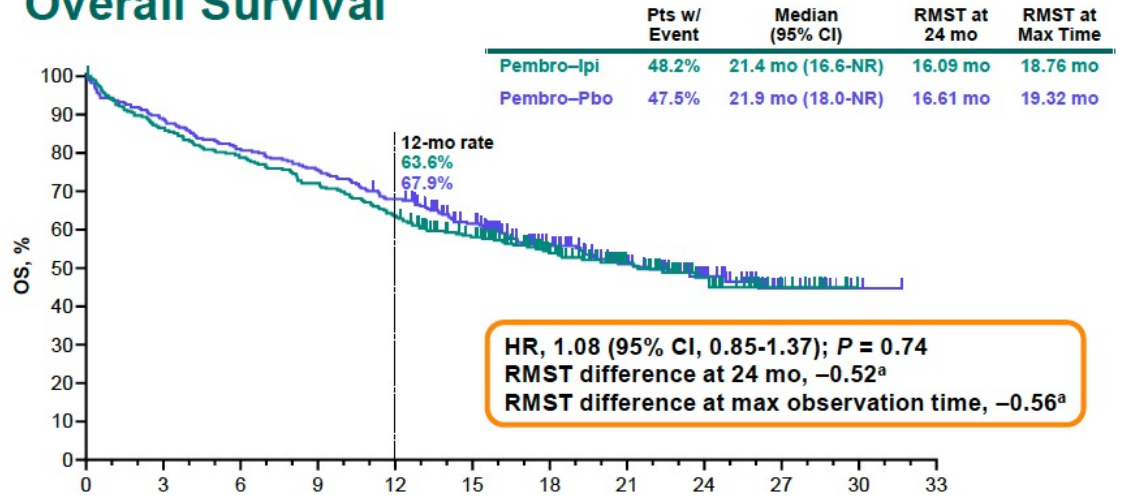
Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

KEYNOTE-598: pembrolizumab et ipilimumab





Overall Survival



Boyer M et al. Abstr PS01.09 WCLC 2020

#1 Immunotherapy to replace chemotherapy

Second line
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Docetaxel

First line
vs.
Platin-based
doublet

Selection on
PD-L1≥50%

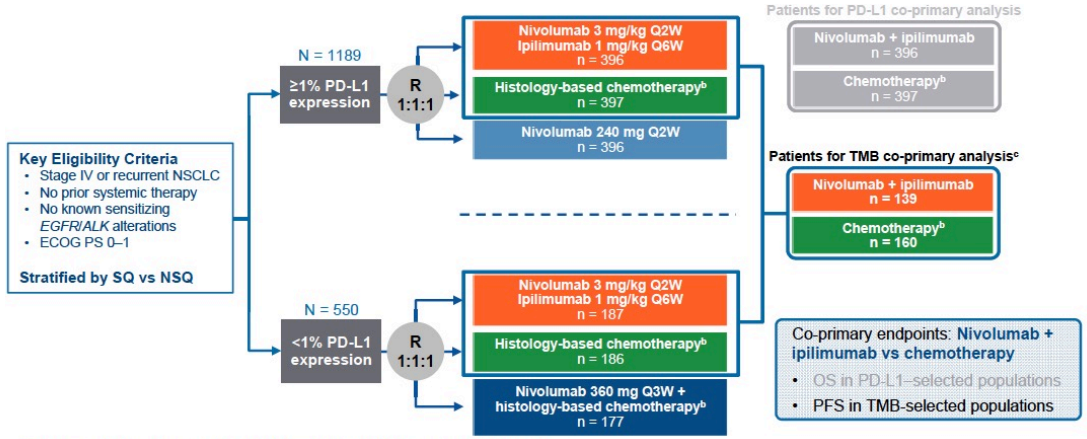
Selection on
lower PD-L1?

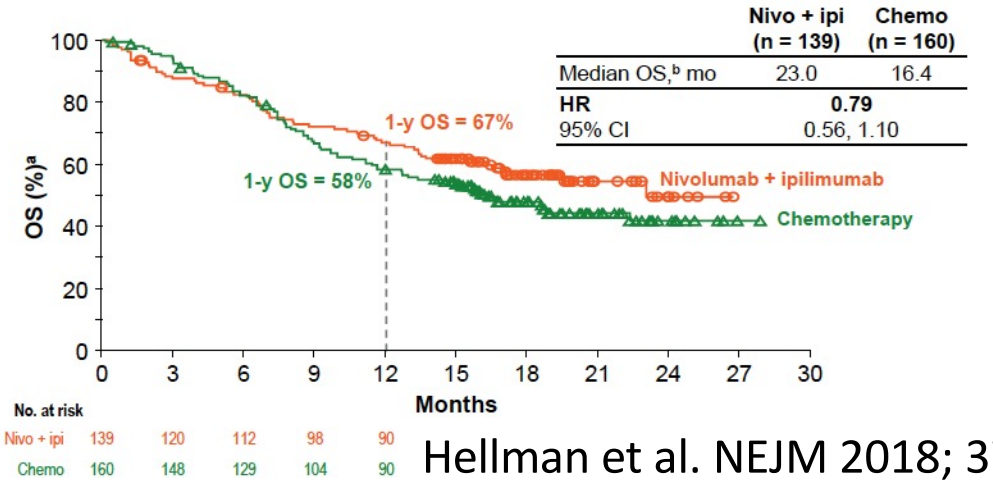
How to
optimise?

Selection on
TMB
≥10 mut/Mb?

Selection based on tumor mutation burden? CHECKMATE-227 and MYSTIC

CHECMATE-227 : nivolumab + ipilimumab (PD-L1≥1%/TMB≥10mut/Mb)

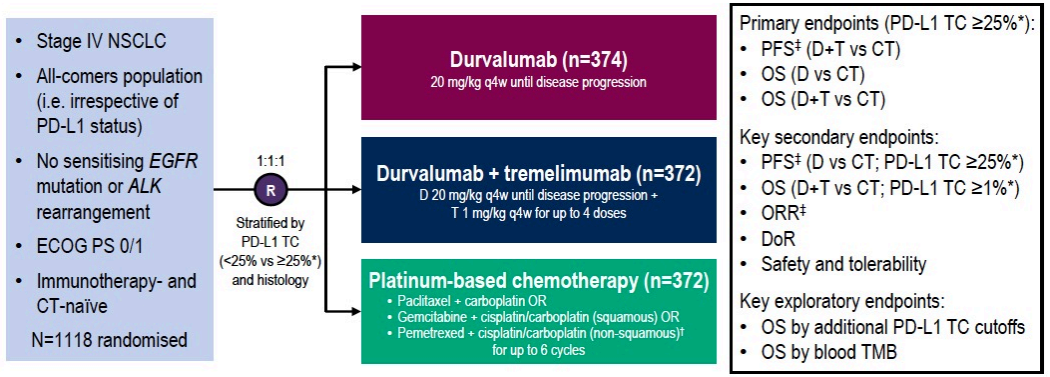


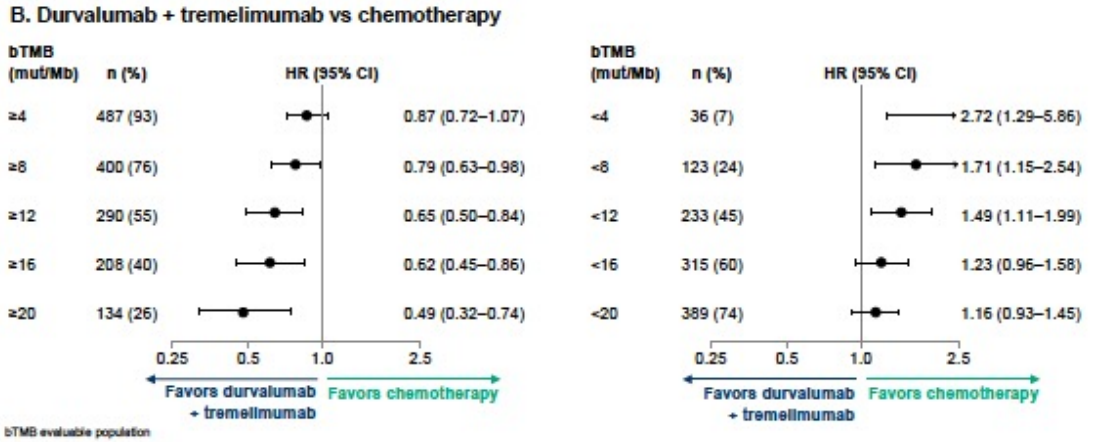


	Nivo + ipi (n = 139)	Chemo (n = 160)
Median OS,[b] mo	23.0	16.4
HR	0.79	
95% CI	0.56, 1.10	

Hellman et al. NEJM 2018; 378:2093

MYSTIC : durvalumab + tremelimumab (PD-L1≥25%)





ASCO 2019

ESMO 2021: B-FAST

Key eligibility criteria
- Unresectable, stage IIIB or IV NSCLC
- Untreated
- ECOG PS 0 or 1
- bTMB+ (bTMB ≥10[a] cutoff)
- Absence of *EGFR/ALK* genetic alteration

R 1:1
n=472[b]

Atezo 1200 mg q3w until PD or loss of clinical benefit

Platinum-based chemo q3w x 4 or 6 cycles (maintenance pemetrexed allowed for nsq NSCLC)

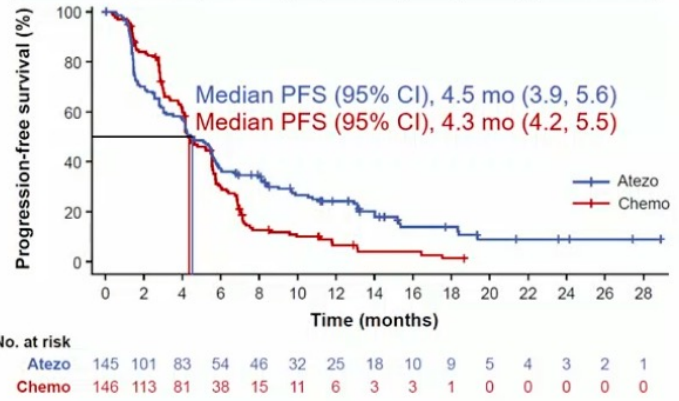
Stratification factors
- **ECOG PS** (0 vs 1)
- **Histology** (sq vs nsq)
- **Tissue availability**[c] (yes vs no)
- **bTMB cutoff status** (moderate [10-15] vs high [≥16])

Primary endpoints
- Investigator-assessed PFS (RECIST 1.1) in bTMB ≥16[d]

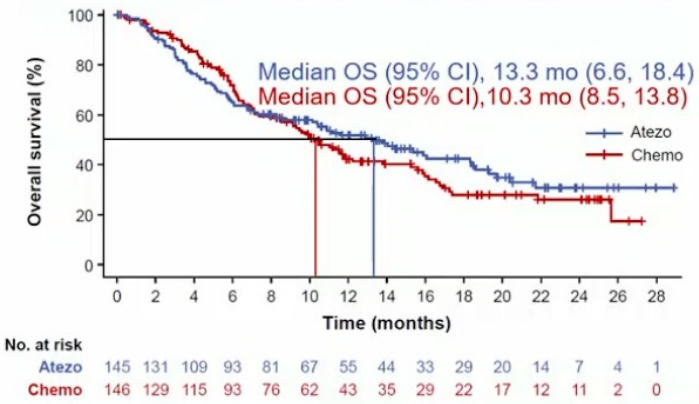
Key secondary endpoints
- OS in bTMB ≥10[a] (ITT) and bTMB ≥16[e]
- Investigator-assessed PFS (RECIST 1.1) in ITT[e]
- Confirmed investigator-assessed ORR and DOR

PFS and OS in the bTMB ≥16 population

	Atezo (n=145)	Chemo (n=146)
PFS events, n (%)	119 (82)	124 (85)
Stratified HR (95% CI)	0.77 (0.59, 1.00); *P*=0.053	



	Atezo (n=145)	Chemo (n=146)
OS events, n (%)	82 (57)	88 (60)
Stratified HR (95% CI)	0.87 (0.64, 1.17); *P*=0.35[a]	



- Although progression rates were initially higher in the atezo vs chemo arm, PFS benefit was seen with atezo after 4 months

Confirmed ORR for bTMB ≥16 was 25.5% (95% CI: 18.7, 33.4) for atezo vs 17.8% (12.0, 25.0) for chemo

Data cutoff, 21 May 2020. Median follow-up, 18.2 mo.
[a] Not formally tested; for descriptive purposes only.

Dziadziuszko et al. BFAST Cohort C.
https://bit.ly/3s4HedG 6

Dziadziuszko et al. ESMO 2021

#2 Immunotherapy in addition to chemotherapy

Immunotherapy *to replace* chemotherapy

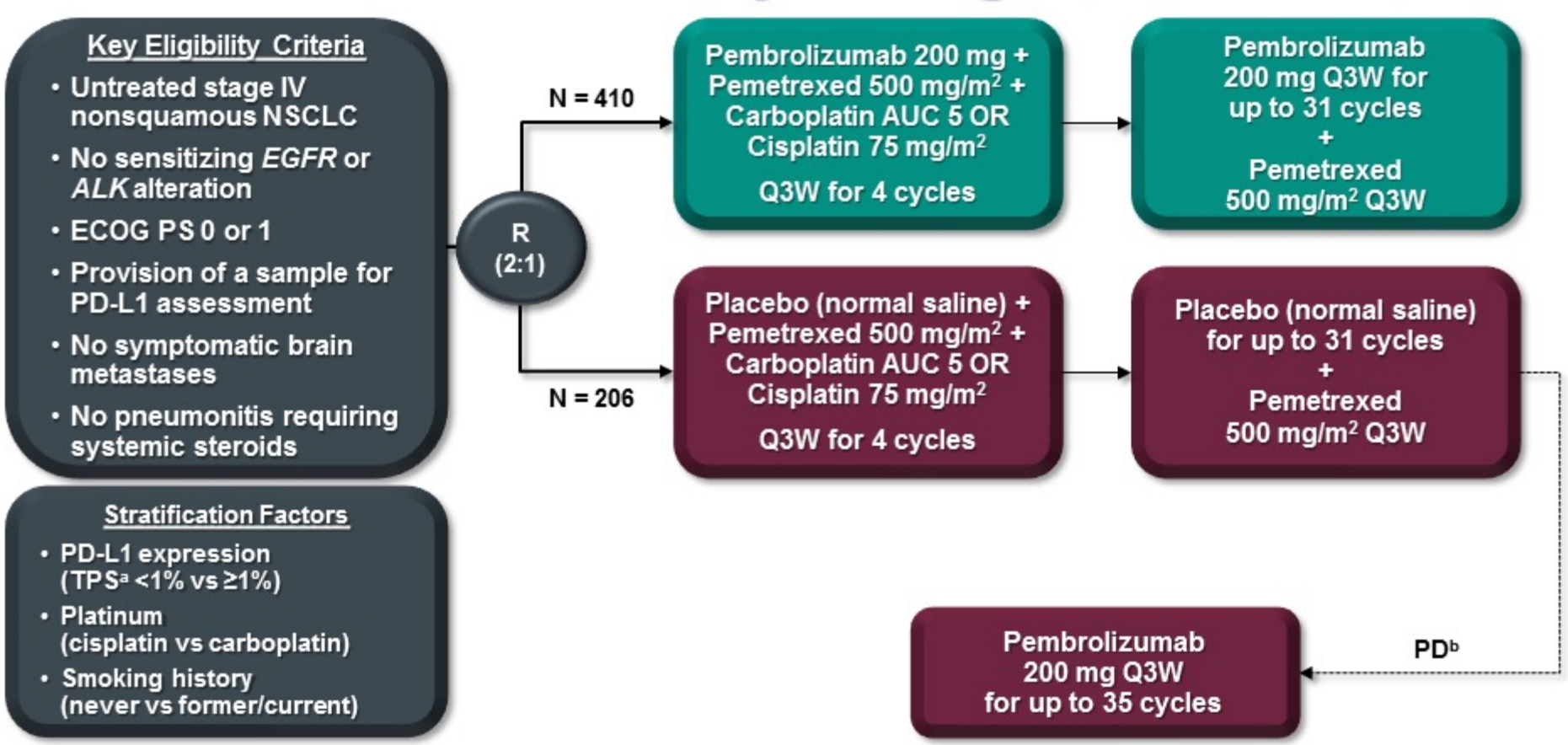
Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

Immunotherapy in addition to chemotherapy Non-squamous cell carcinomas

Placebo
Stratification on PD-L1
Exclusion of EGFR/ALK

KEYNOTE-189: design



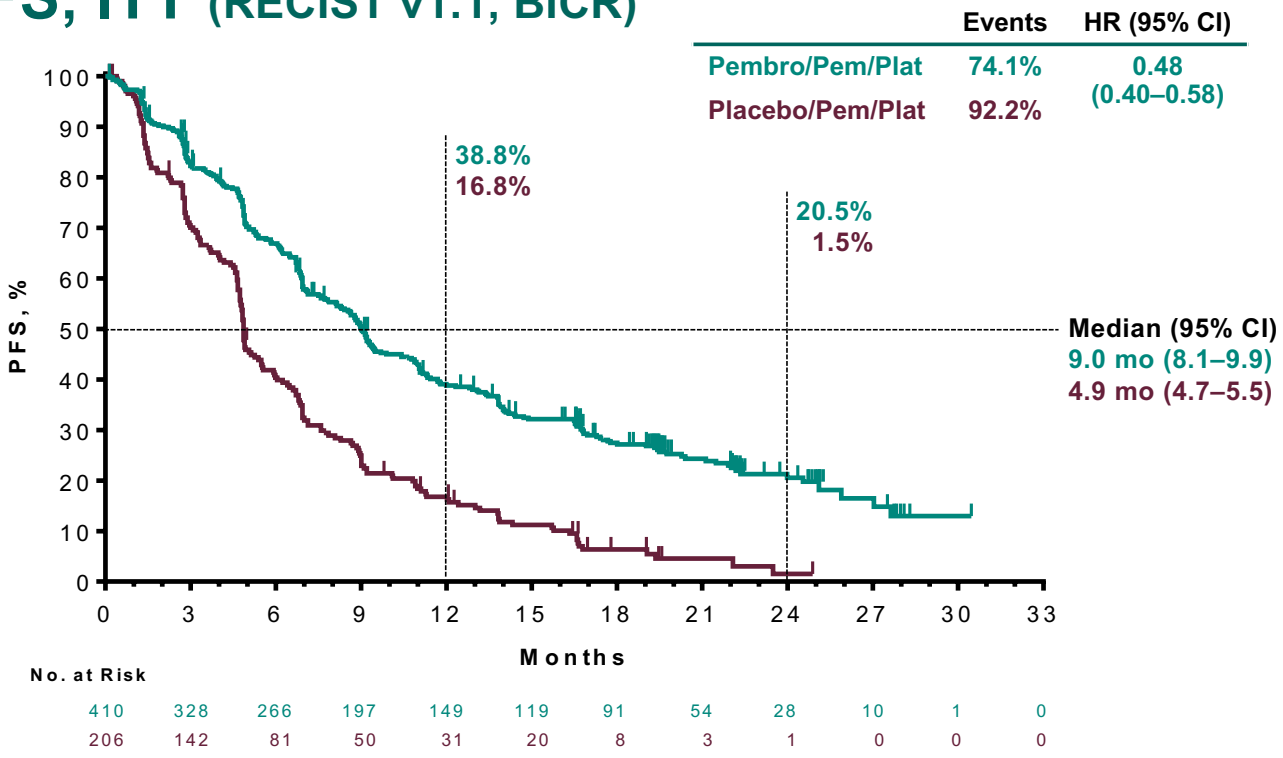
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during the induction or maintenance phases. To be eligible for crossover, PD must have been verified by blinded, independent central radiologic review and all safety criteria had to be met.

Gandhi et al. NEJM 2018;378:2078

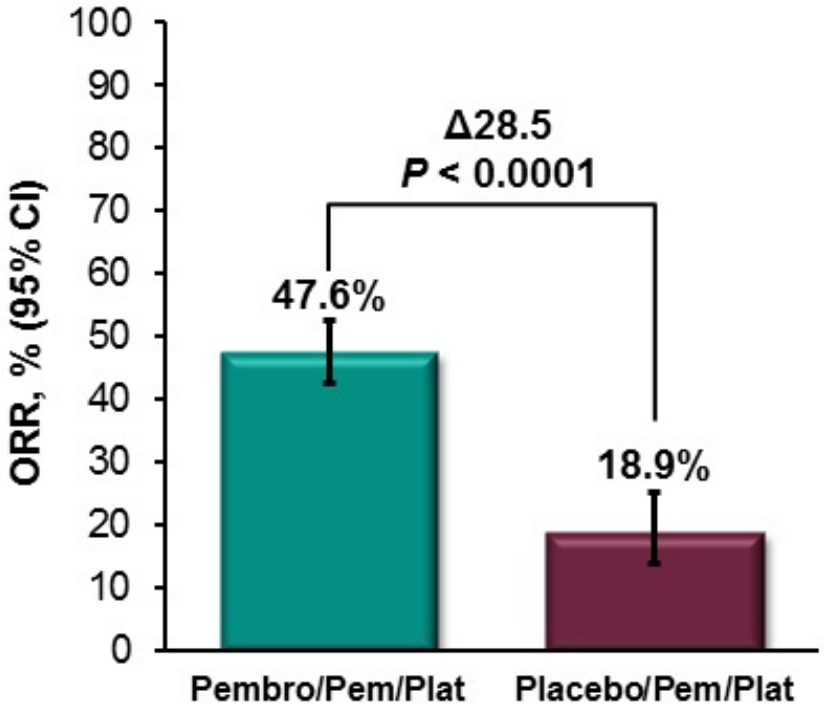
Immunotherapy in addition to chemotherapy Non-squamous cell carcinomas

KEYNOTE-189: results

PFS, ITT (RECIST v1.1, BICR)



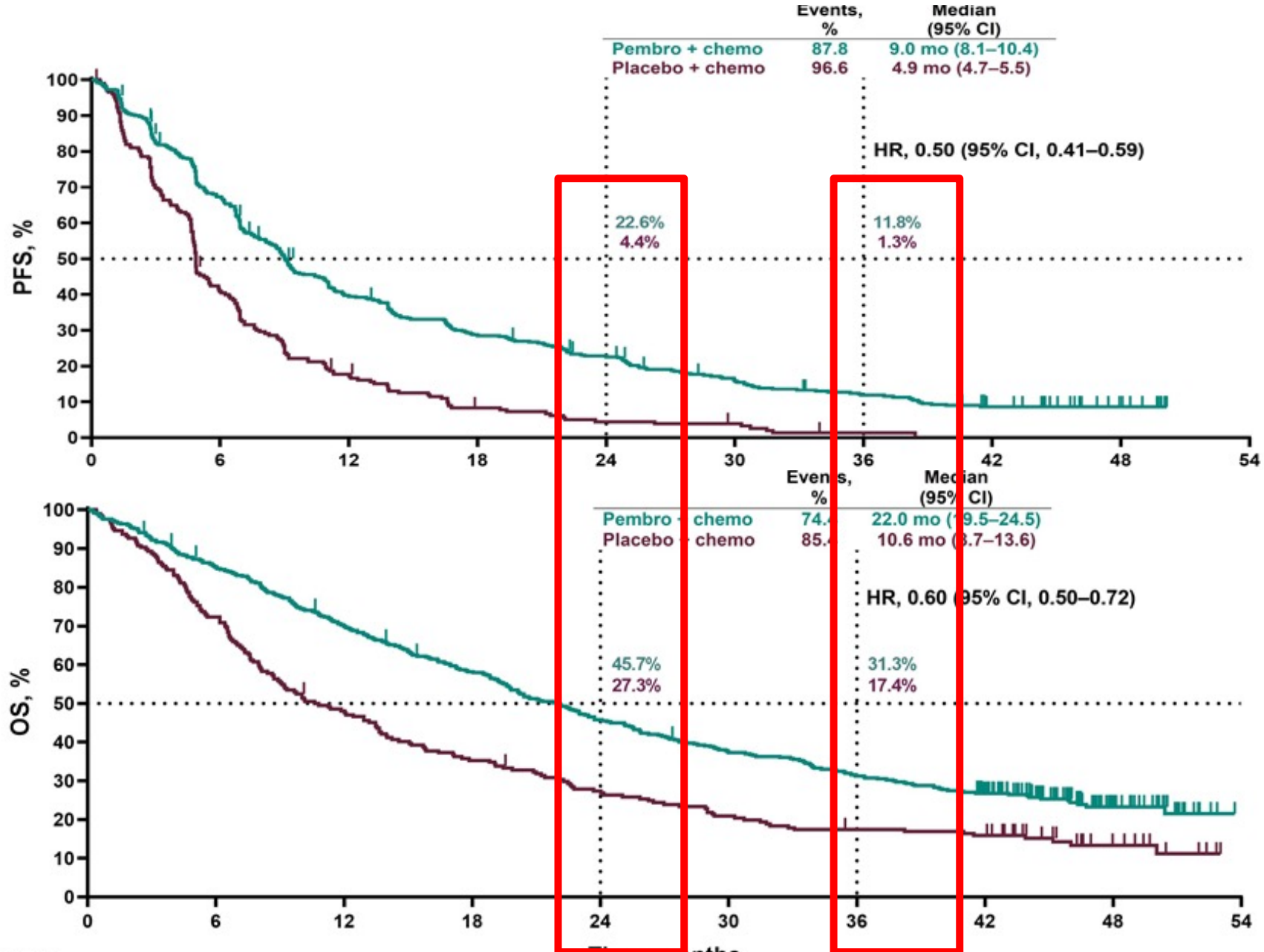
BICR, blinded, independent central review. Data cutoff date: Sep 21, 2018.



Gadgeel et al. ASCO 2019

Immunothérapie en combinaison avec la chimiothérapie Non-épidermoïdes

KEYNOTE-189: résultats

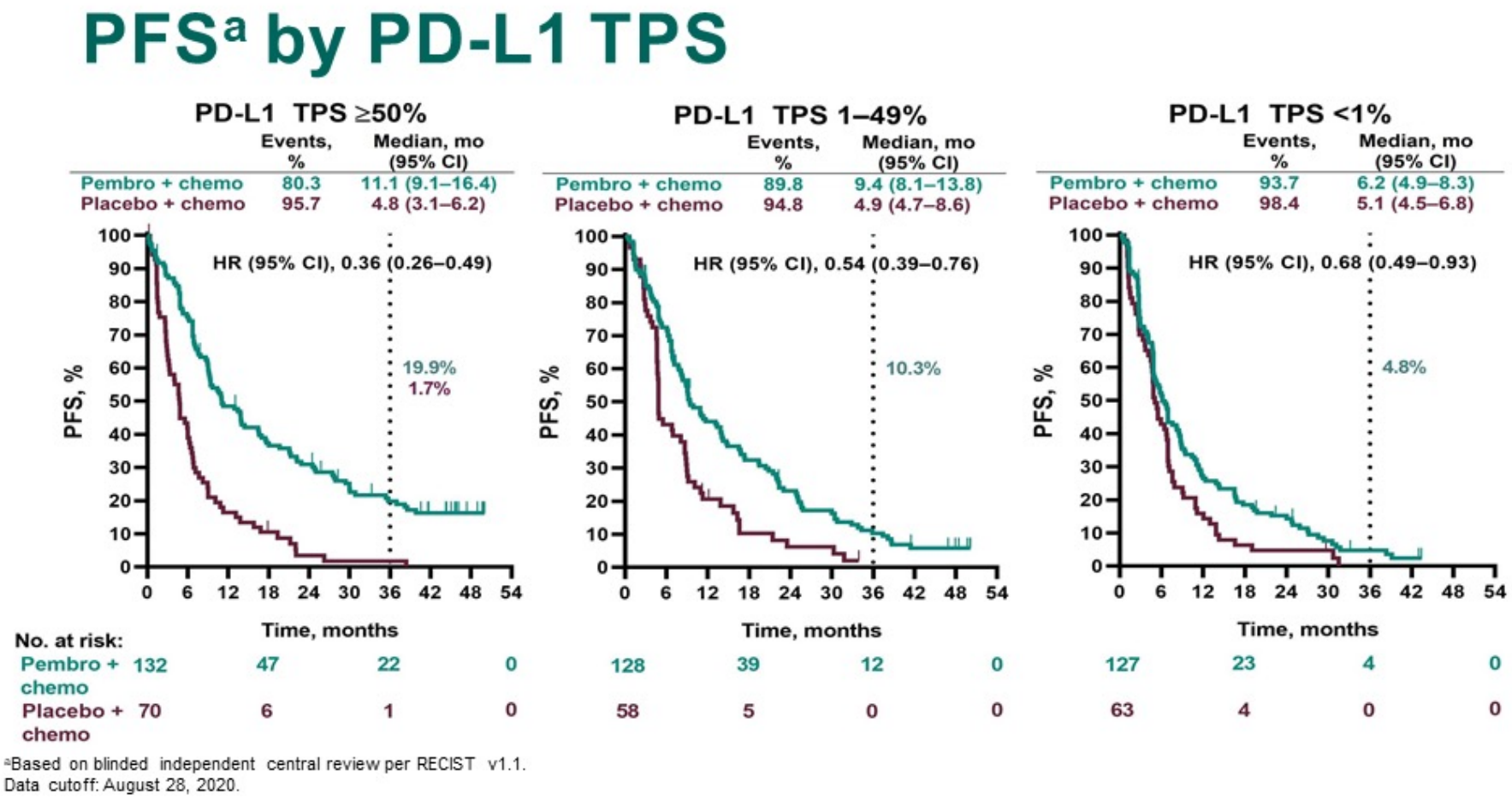


Gray JE et al. Abstr FP13.02 WCLC 2020

Immunothérapie en combinaison avec la chimiothérapie Non-épidermoïdes

KEYNOTE-189: résultats

Gray MK-3475 KN189 WCLC 2020



Gray JE et al. Abstr FP13.02 WCLC 2020

#2 Immunotherapy in addition to chemotherapy

Immunotherapy *to replace* chemotherapy

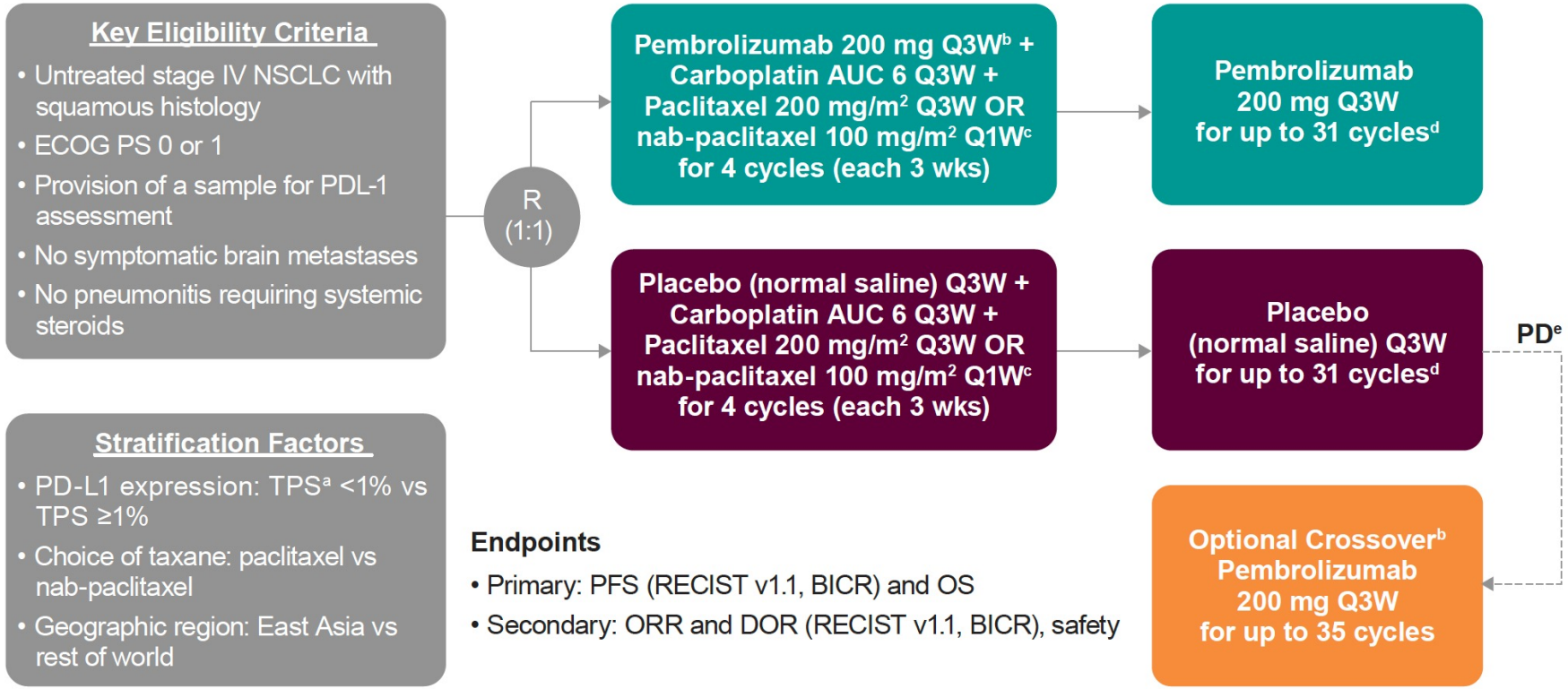
Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

Immunotherapy in addition to chemotherapy Squamous cell carcinomas

Placebo
Stratification on PD-L1

KEYNOTE-407: design



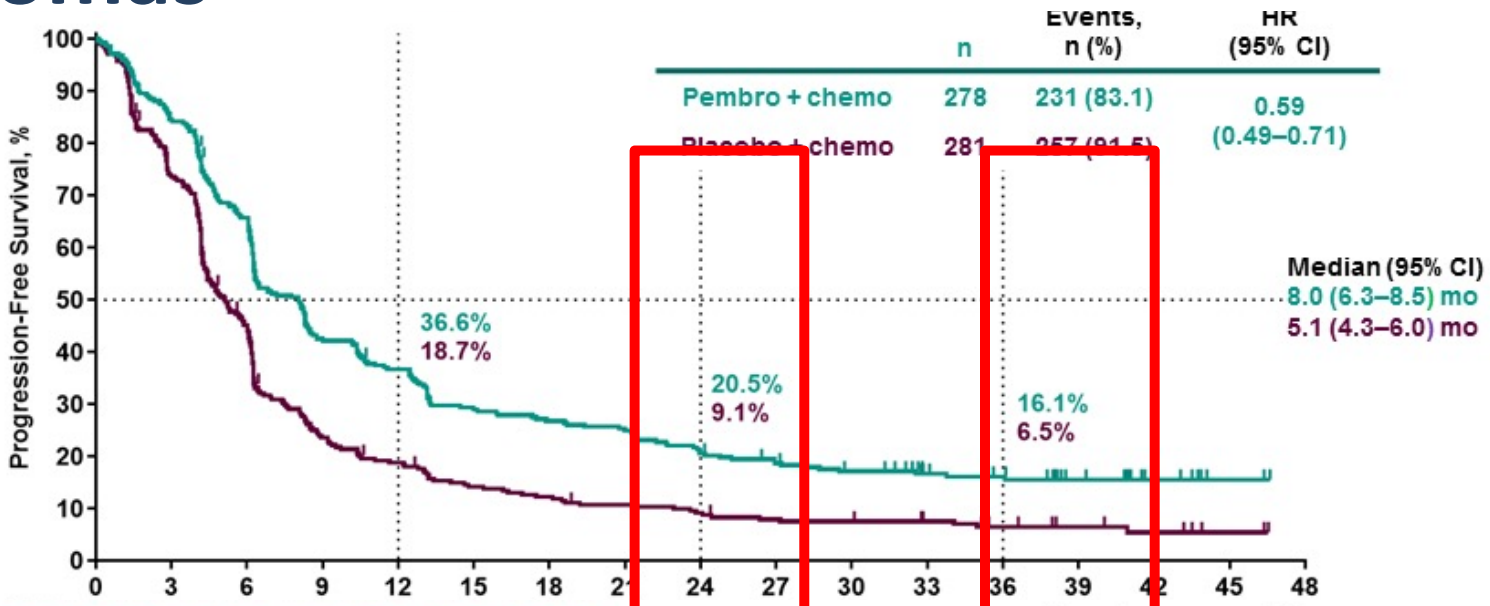
AUC, area under the curve; BICR, blinded independent central review; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; Q1W, every week; Q3W, every 3 weeks; R, randomization; TPS, tumor proportion score.
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA).
[b]Patients with documented disease progression who were benefiting clinically could continue open-label pembrolizumab monotherapy to complete a total of 35 cycles.

Paz-Ares et al. ESMO 2019

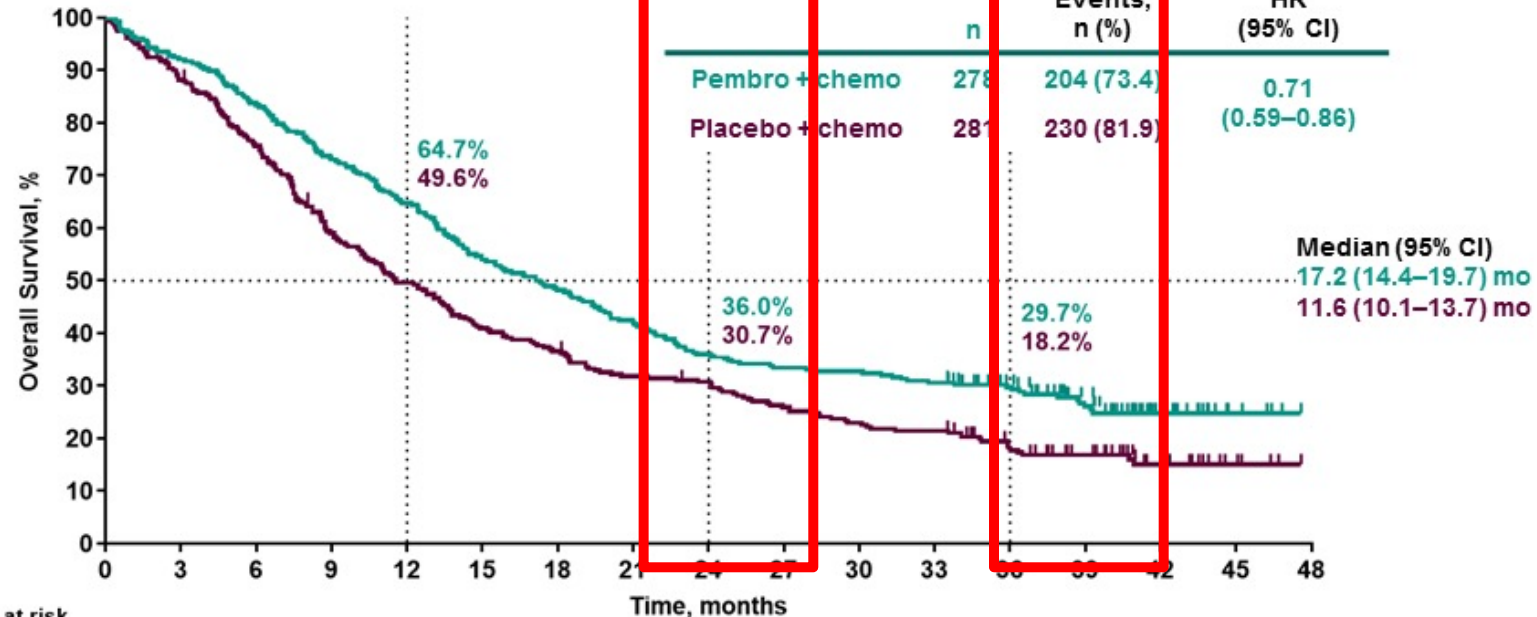
Immunotherapy in addition to chemotherapy
Squamous cell carcinomas

KEYNOTE-407: results

Progression-free survival



Overall Survival



Robinson et al. ELCC 2021

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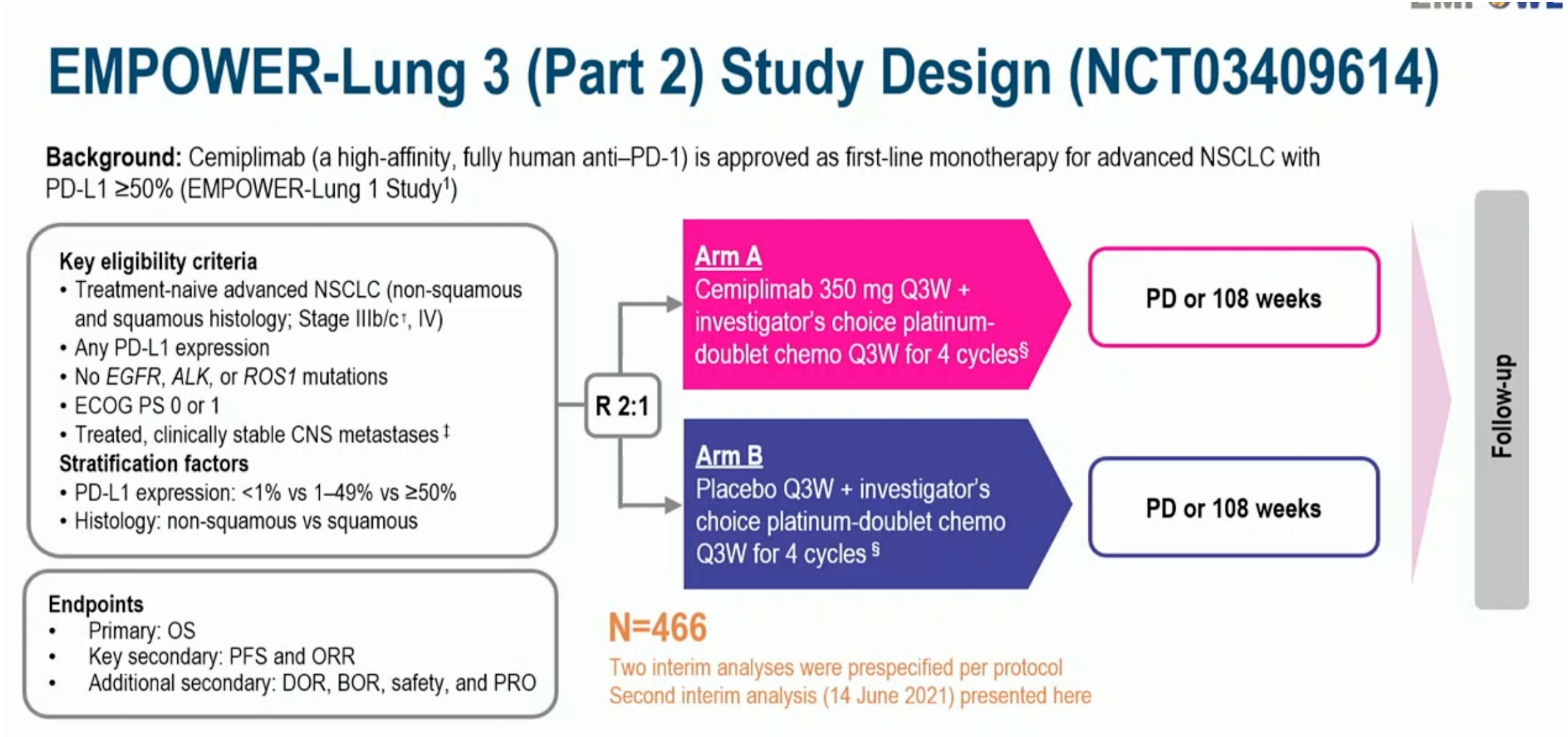
Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

Immunotherapy in addition to chemotherapy EMPOWER LUNG 3



Goguishvili et al. ESMO 2021

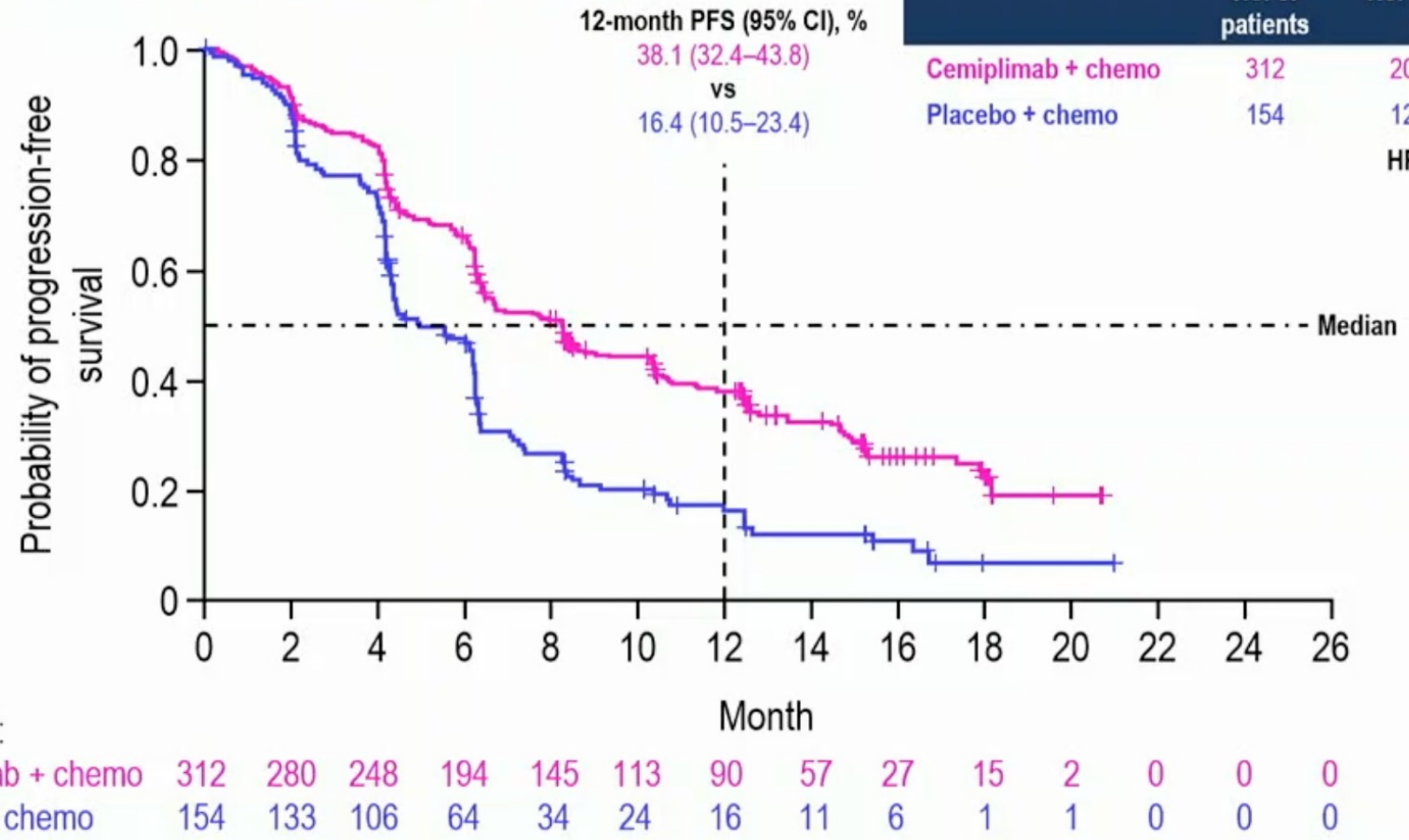
Immunotherapy in addition to chemotherapy EMPOWER LUNG 3

Progression-Free Survival

Median duration of follow-up (range): 16.4 (8.5–24.0) months

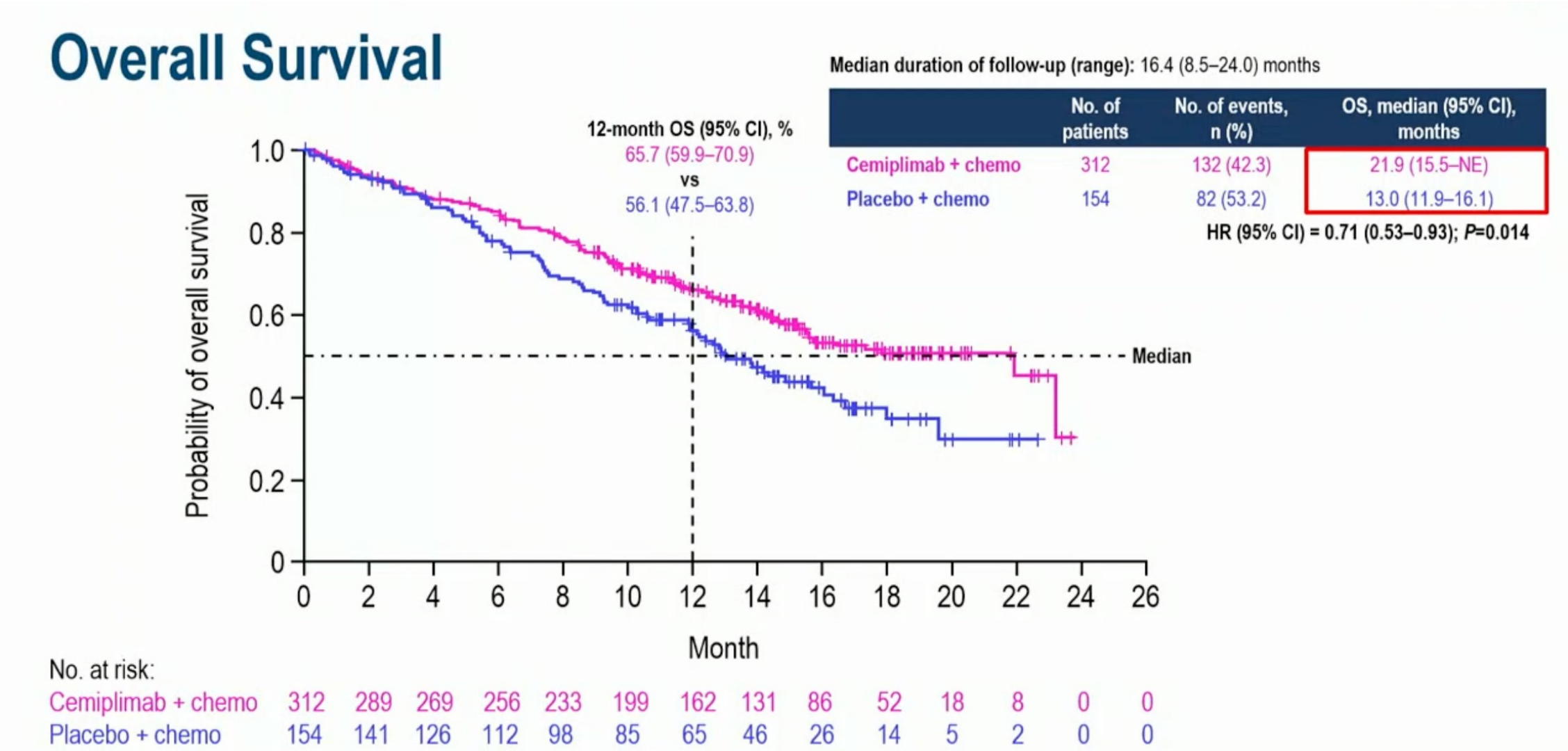
	No. of patients	No. of events, n (%)	PFS, median (95% CI), months
Cemiplimab + chemo	312	204 (65.4)	8.2 (6.4–9.3)
Placebo + chemo	154	122 (79.2)	5.0 (4.3–6.2)

HR (95% CI) = 0.56 (0.44–0.70); *P*<0.0001



Goguishvili et al. ESMO 2021

Immunotherapy in addition to chemotherapy EMPOWER LUNG 3



Goguishvili et al. ESMO 2021

#2 Immunotherapy in addition to chemotherapy

Immunotherapy *to replace* chemotherapy

Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

ASCO 2021: CheckMate-9LA

CheckMate 9LA study design[a]

Key Eligibility Criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0-1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%), sex, and histology (SQ vs NSQ)

N = 719

R 1:1

n = 361: **NIVO** 360 mg Q3W + **IPI** 1 mg/kg Q6W + **Chemo[d]** Q3W (2 cycles)

n = 358: **Chemo[d]** Q3W (4 cycles) with optional pemetrexed maintenance (NSQ)

Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint
- OS

Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

Interim database lock: October 3, 2019; minimum follow-up: 8.1 months for OS and 6.5 months for all other endpoints.
Updated database lock: March 9, 2020; minimum follow-up: 12.7 months for OS and 12.2 months for all other endpoints.

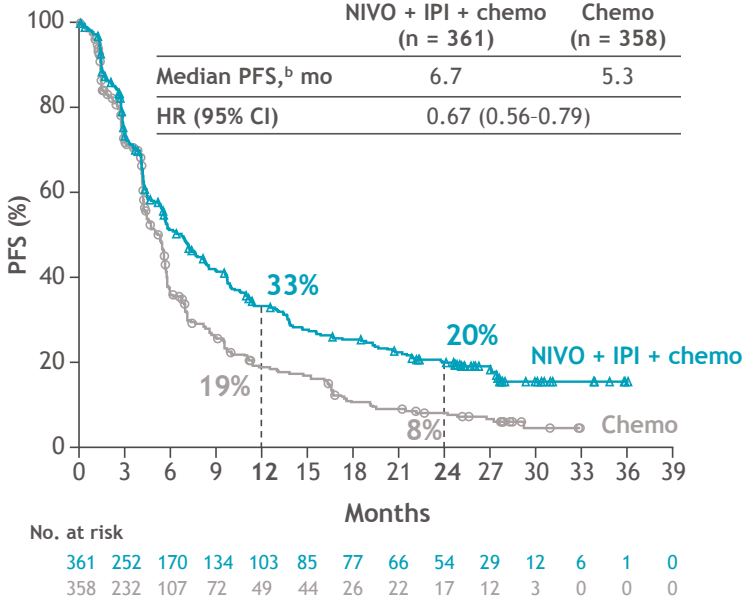
[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]**NSQ**: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

Reck, et al. ASCO 2021

ASCO 2021: CheckMate-9LA

2-Year update: PFS and DOR

PFS[a]



	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median PFS,[b] mo	6.7	5.3
HR (95% CI)	0.67 (0.56-0.79)	

No. at risk

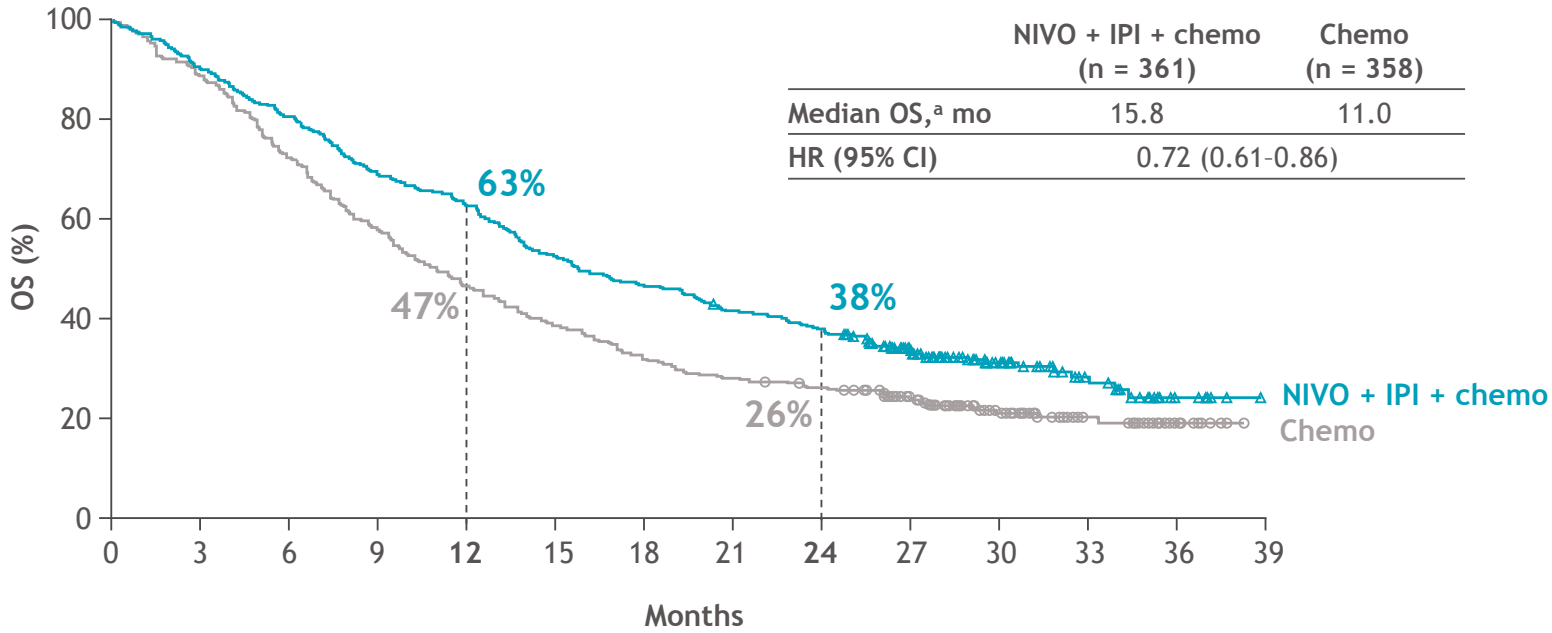
NIVO + IPI + chemo	361	252	170	134	103	85	77	66	54	29	12	6	1	0
Chemo	358	232	107	72	49	44	26	22	17	12	3	0	0	0

Minimum follow-up: 23.3 months.
[a]Per BICR; [b]95% CI = 5.6-7.8 (NIVO + IPI + chemo) and 4.4-5.6 (chemo); [c]Includes 3.3% CR and 34.6% PR; 4 patients improved to CRs; [d]Includes 1.1% CR and 24.3% PR; [e]95% CI = 8.7-20.2 (NIVO + IPI + chemo) and 4.4-7.2 (chemo).

DOR[a]

CheckMate 9LA (NIVO + IPI + chemo vs chemo in 1L NSCLC): 2-year update

2-Year update: OS in all randomized patients



	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS,[a] mo	15.8	11.0
HR (95% CI)	0.72 (0.61-0.86)	

No. at risk

NIVO + IPI + chemo	361	326	292	250	227	191	170	150	137	95	50	23	7	0
Chemo	358	319	260	208	168	139	115	102	93	69	40	18	8	0

Minimum follow-up: 24.4 months.
[a]95% CI = 13.9-19.7 (NIVO + IPI + chemo) and 9.5-12.7 (chemo).

Reck, et al. ASCO 2021

#2 Immunotherapy in addition to chemotherapy

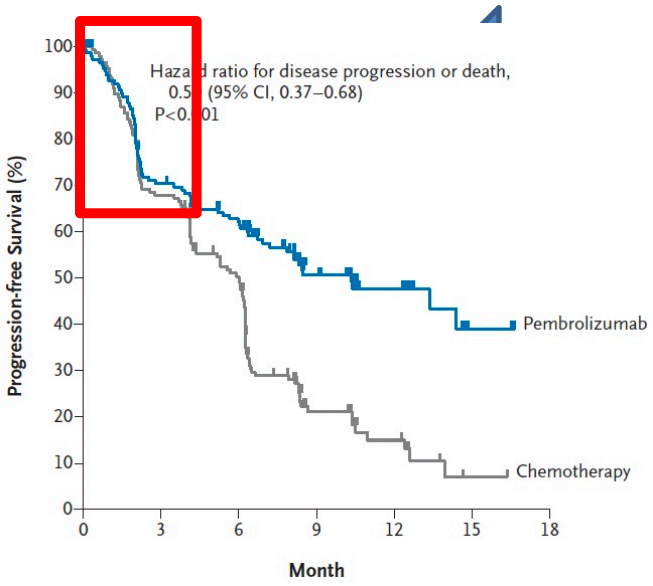
Immunotherapy to replace chemotherapy

Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

PD-L1≥50%
Question: pembrolizumab alone or with chemotherapy or nivolumab plus ipilimumab?

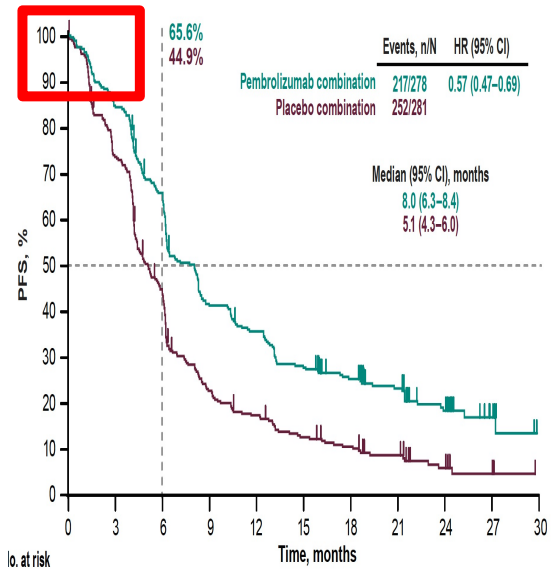
Pembrolizumab alone
All histologies



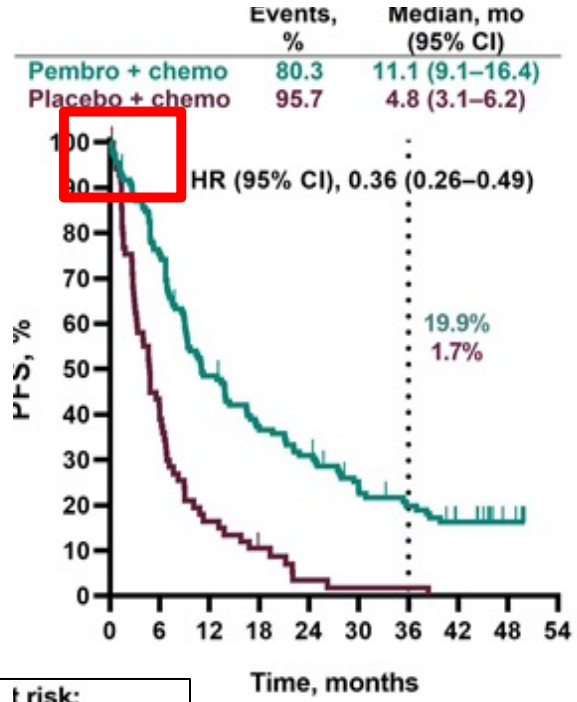
30% early PD

Pembrolizumab plus chemo

Squamous

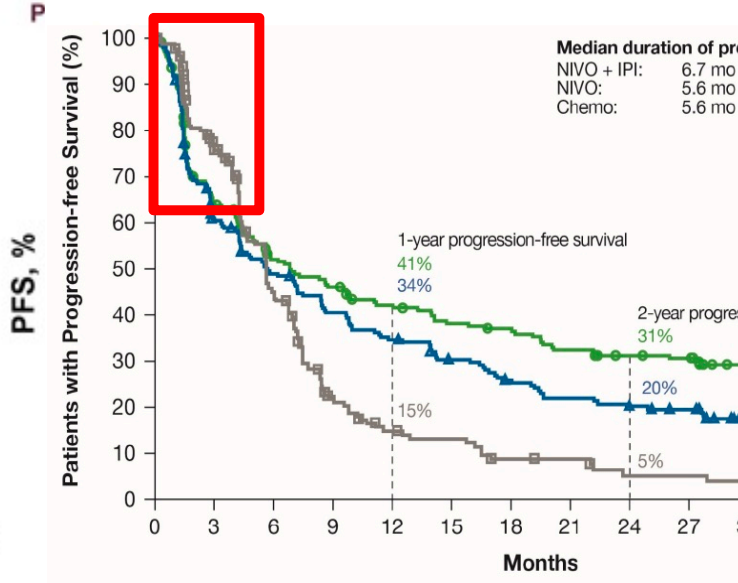


Non-Squamous



10% early PD

Nivolumab + ipilimumab
All histologies

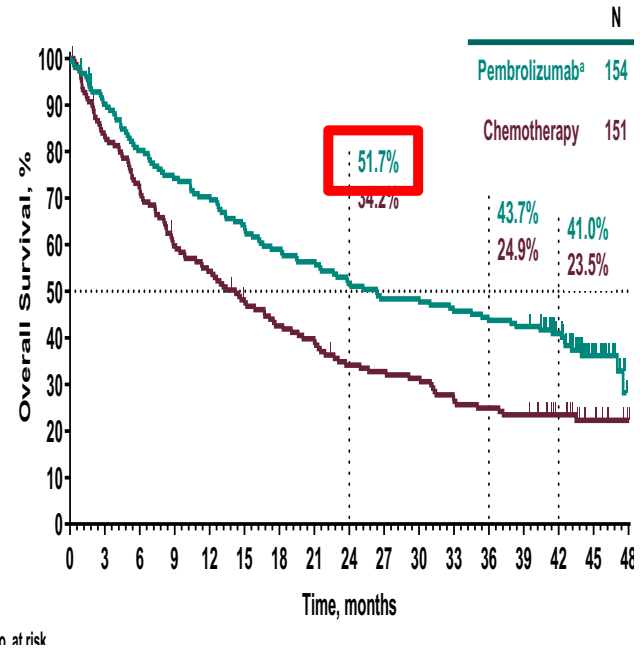


30% early PD

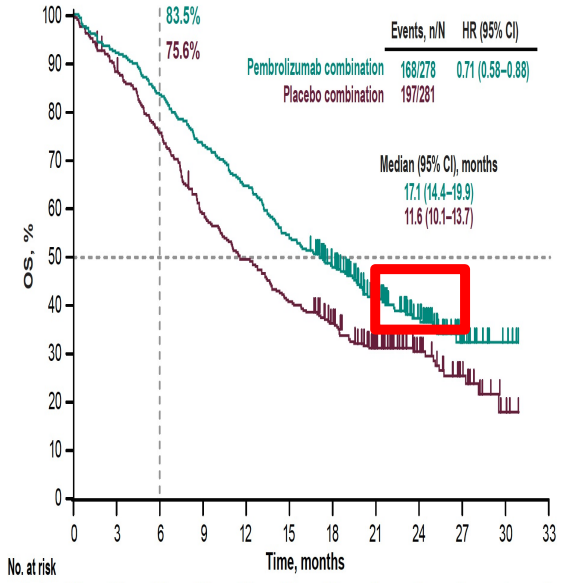
Reck et al. WCLC 2019; Gfadgeel et al. ASCO 2019; Reck et al. NEJM 2016;375:1823; Paz-Ares et al. ESMO 2019; Peters et al. ESMO 2019

PD-L1≥50%
Question: pembrolizumab alone or with chemotherapy or nivolumab plus ipilimumab?

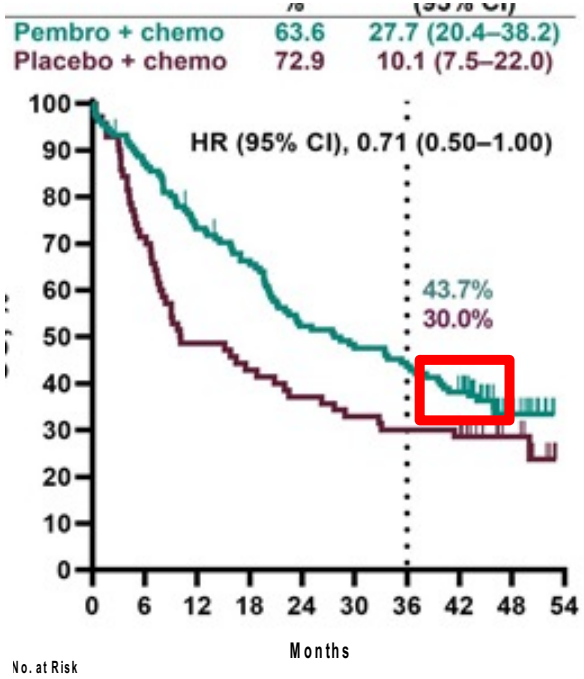
Pembrolizumab alone
All histologies



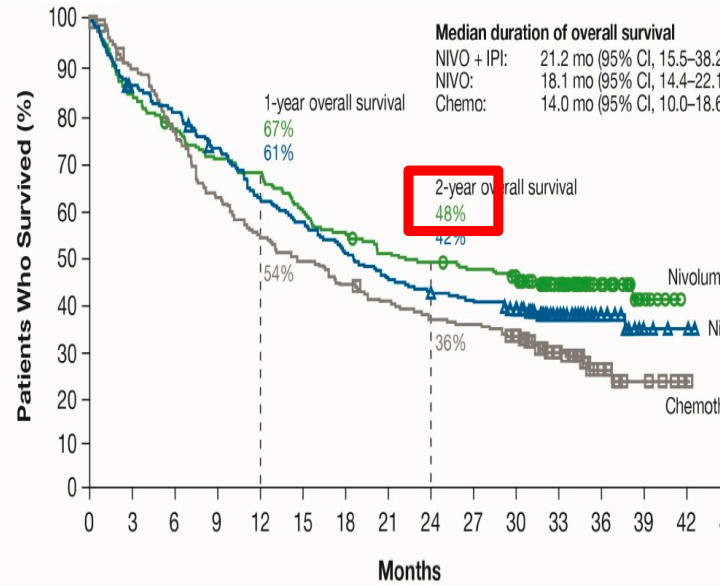
Pembrolizumab plus chemo
Squamous



Pembrolizumab plus chemo
Non-Squamous



Nivolumab + ipilimumab
All histologies



Reck et al. WCLC 2019; Gfadgeel et al. ASCO 2019; Reck et al. NEJM 2016;375:1823; Paz-Ares et al. ESMO 2019; Peters et al. ESMO 2019

#2 Immunotherapy in addition to chemotherapy

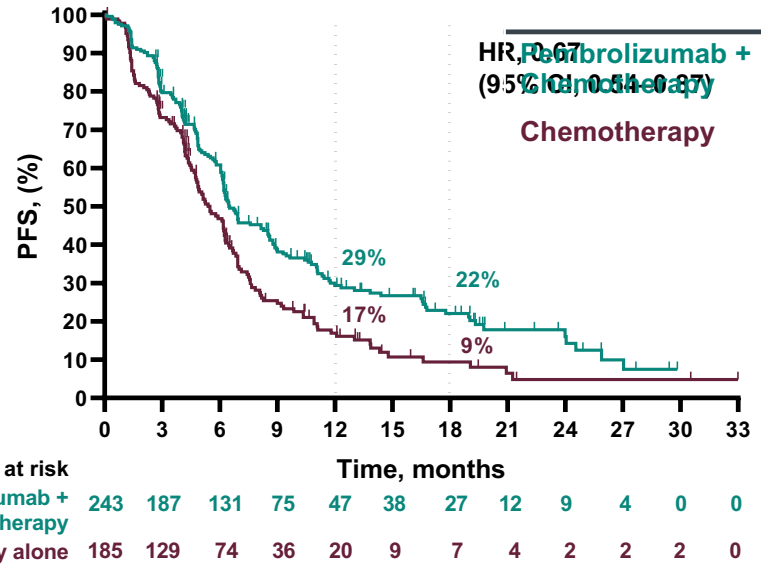
Immunotherapy to replace chemotherapy

Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

Prediction of efficacy: PD-L1 expression
Exploratory analyses in PD-L1 negative

KEYNOTE—407, -21G, -189

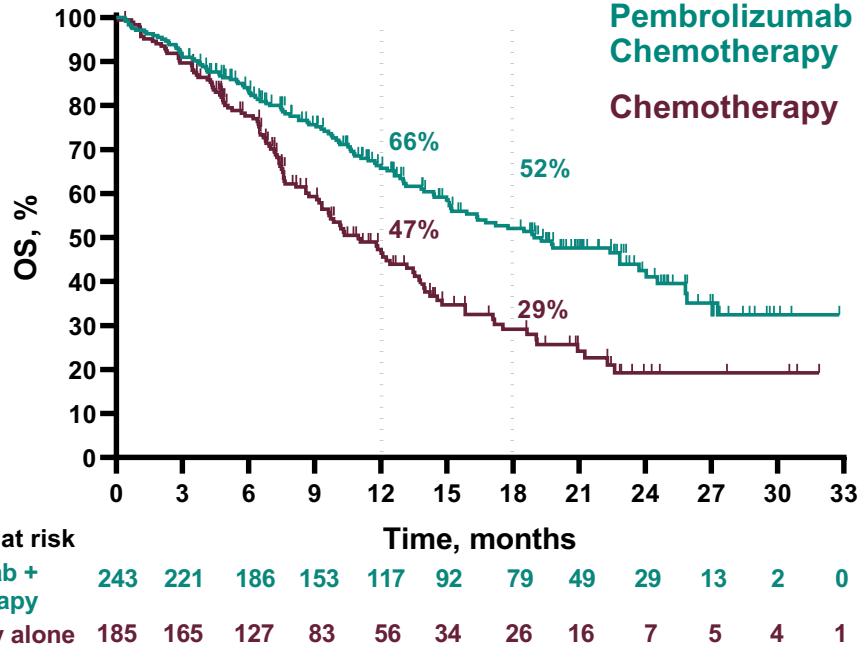


	Events, n	HR (95% CI)
Pembrolizumab + Chemotherapy	172	0.67 (0.54–0.84)
Chemotherapy	145	

Median (95% CI) PFS

6.5 (6.2–8.5) mo

5.4 (4.7–6.2) mo



	Events, n	HR (95% CI)
Pembrolizumab + Chemotherapy	112	0.56 (0.43–0.73)
Chemotherapy	110	

Median (95% CI) OS

19.0 (15.2–24.0) mo

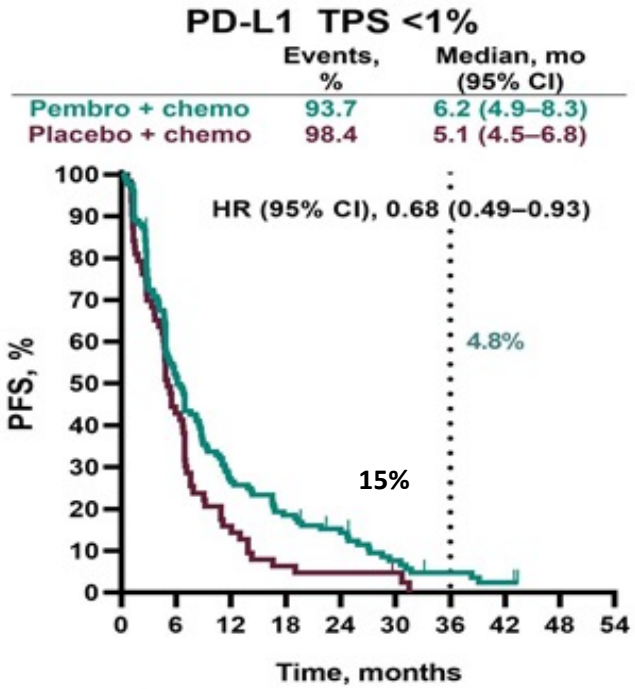
11.0 (9.2–13.5) mo

Borghaei et al. WCLC 2019 OA14.01

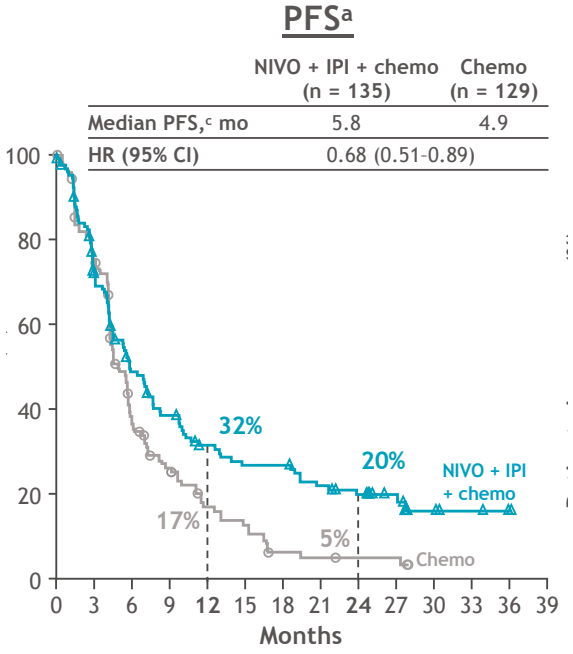
ASCO 2021: CheckMate-9LA
PD-L1 négatifs

Survie sans progression

KEYNOTE-189

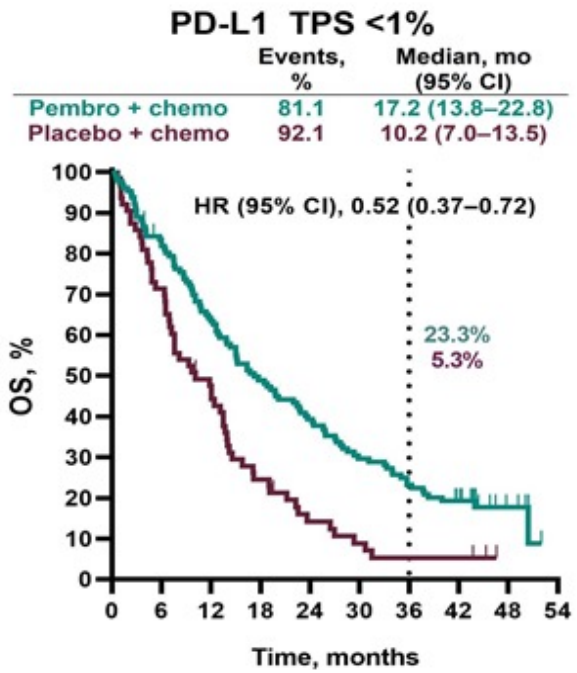


CheckMate-9LA

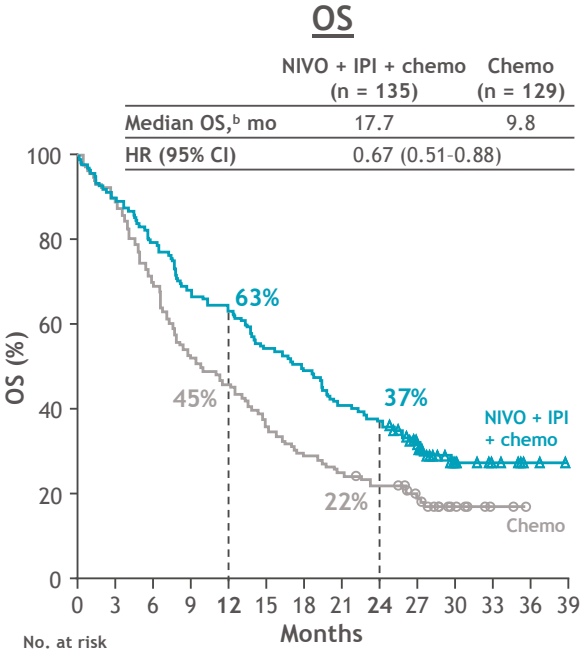


Survie globale

KEYNOTE-189



CheckMate-9LA



Gray et al. WCLC 2020
Reck et al. ASCO 2021

#2 Immunotherapy in addition to chemotherapy

Immunotherapy to replace chemotherapy

Immunotherapy *in addition* to chemotherapy

Immunotherapy *after* chemoradiotherapy

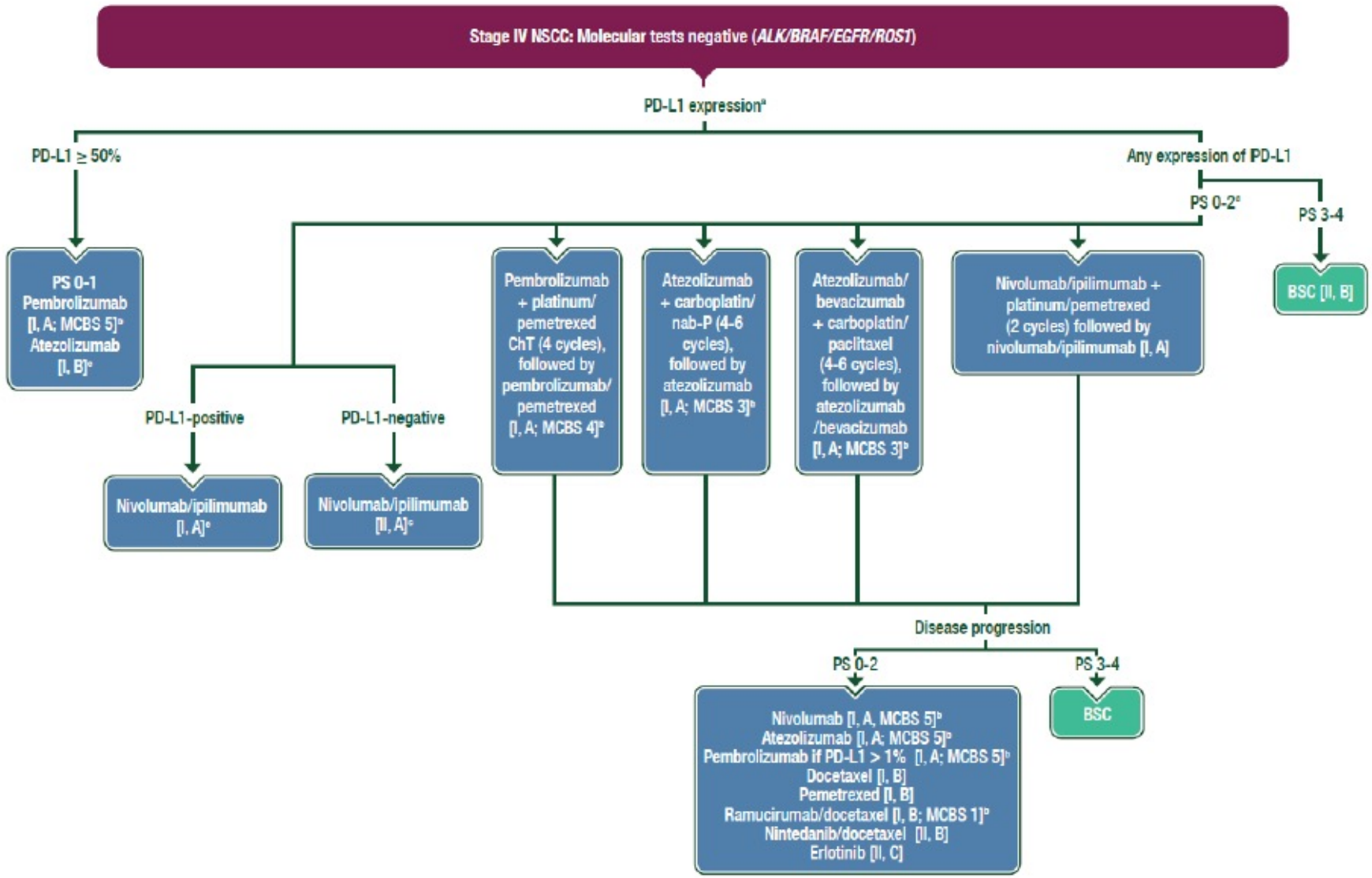
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Updated version published 15 September 2020 by the ESMO Guidelines Committee

CLINICAL PRACTICE GUIDELINES

Metastatic non-small cell lung canc
Guidelines for diagnosis, treatment

Originally published in 2018 – Ann Oncol (2018) 29(
D. Planchard[1], S. Popat[2], K. Kerr[3], S. Novello[4], E. F.
Reck[8], P. E. Van Schil[9], M. D. Hellmann[10] & S. Pete
Committee*



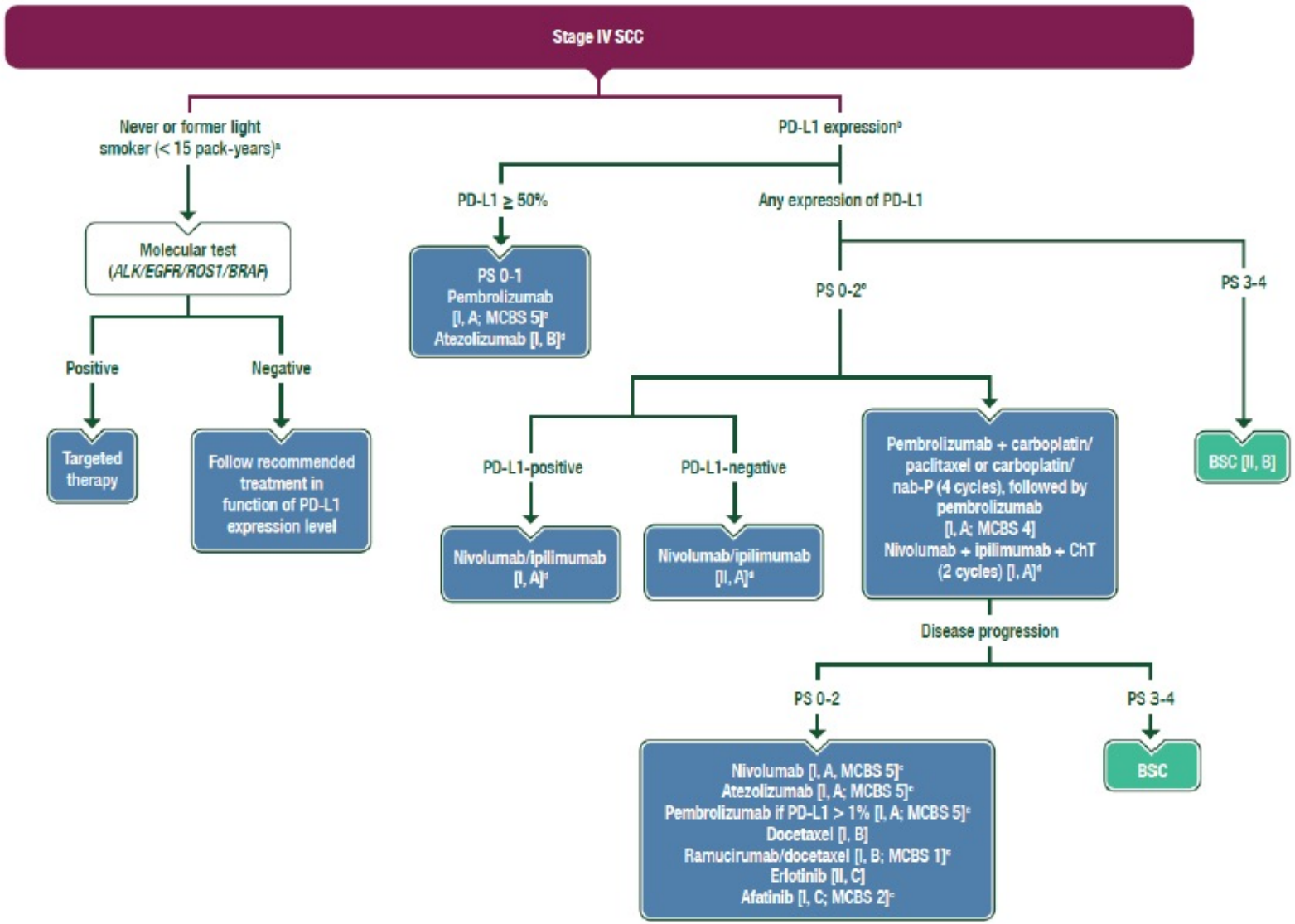
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Updated version published 15 September 2020 by the ESMO Guidelines Committee

CLINICAL PRACTICE GUIDELINES

Metastatic non-small cell lung cancer: ESM Clinical Practice Guidelines for diagnosis, treatment and fo

Originally published in 2018 – Ann Oncol (2018) 29(Suppl 4): iv
D. Planchard[1], S. Popat[2], K. Kerr[3], S. Novello[4], E. F. Smit[5], C. Reck[8], P. E. Van Schil[9], M. D. Hellmann[10] & S. Peters[11], on beh Committee*



Post-IO stratégies?

Targeted
KRAS, BRAF, HER2…

Docetaxel
Single agent chemos

Rechallenge

New targets for non oncogene addicted tumors
TNF, CEACAM, TROP-2, HLA-A2, MET

ESMO 2021: TEDOPI

- Advanced/metastatic NSCLC
- EGFRwt, ALK-negative, all PD-L1 status
- HLA-A2+ (blood)
- Failure to platinum-based CT and IO, combined or sequenced
- IO last line with primary or secondary resistance*
- Brain metastases allowed if asymptomatic & treated
- ECOG PS 0 to 1

R 2:1

Arm A: OSE2101 Q3W for 6 subcutaneous injections, then Q8W up to Year 1, then Q12W until progression or toxicity

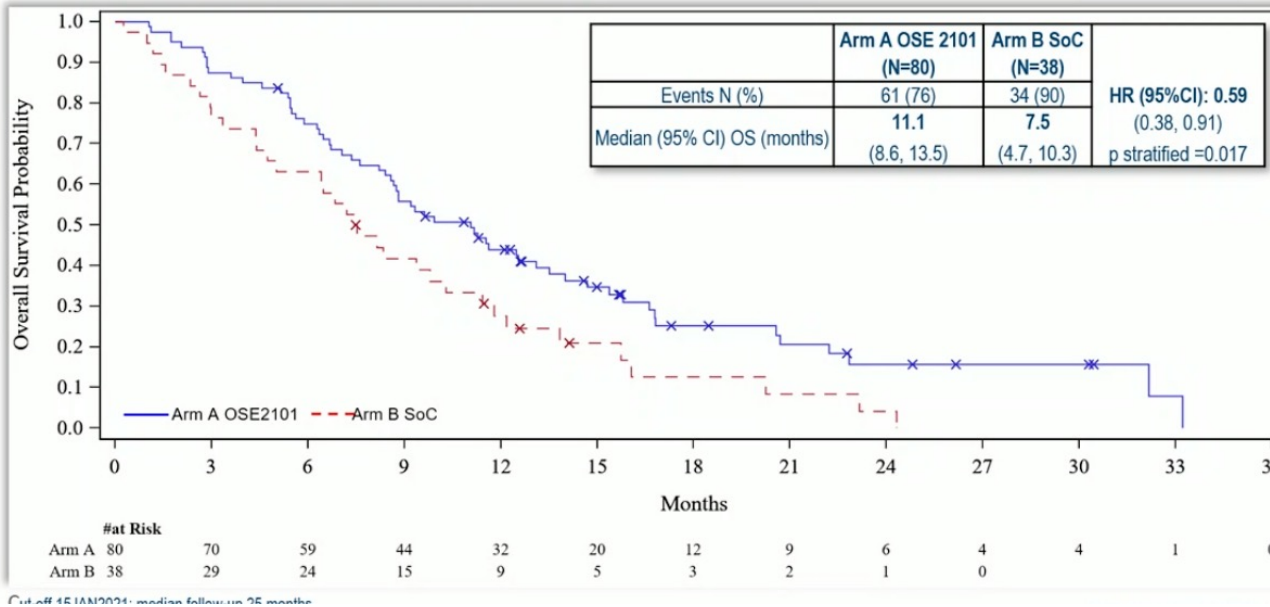
Arm B: SoC (docetaxel or pemetrexed) Q3W until progression or toxicity

Primary endpoint: OS

Stratification:
- Histology
- Best response to 1st line
- Line rank of prior IO

- Step-1 primary endpoint was achieved (cut off February 2020; 103 patients)[1]:
  1-year OS rate 46% versus 36% in SoC (Fleming design); HR for OS=0.71
- Due to the risk of COVID-19 on data integrity, the study was prematurely stopped in April 2020 upon the Independent Data Monitoring Committee recommendation:
  219 pts instead of initial ≈400 pts were enrolled
- Population of Interest (PoI) was identified from Step-1:
  patients with IO secondary resistance after sequential IO; HR for OS=0.65
- PoI and revision of statistical plan were discussed with FDA in July 2021 before database lock
- The final primary analysis was done in the PoI:
  the initial hypothesis of 278 events for HR 0.7 was not reachable
  revised statistical hypothesis in PoI: 90 events for HR=0.55; power 80%, 2-sided level of 5%

Overall Survival in PoI



	Arm A OSE 2101 (N=80)	Arm B SoC (N=38)	
Events N (%)	61 (76)	34 (90)	HR (95%CI): 0.59 (0.38, 0.91) p stratified =0.017
Median (95% CI) OS (months)	11.1 (8.6, 13.5)	7.5 (4.7, 10.3)	

Cut-off 15 JAN2021; median follow-up 25 months

Besse et al. ESMO 2021

ESMO 2021: canakimumab

CANOPY-2: A Phase III RCT of 2/3L canakinumab in combination with docetaxel in advanced/metastatic NSCLC

Key eligibility criteria:

- Adults with stage IIIB or IV NSCLC[a]
- SQ or NSQ histology
- No *EGFR* mutation or *ALK* rearrangement
- ECOG PS ≤1
- Previously treated with 1 platinum-based chemotherapy and 1 PD-(L)1 inhibitor either in combination or sequentially

N=237
R 1:1

- Canakinumab 200 mg SC Q3W + docetaxel 75 mg/m² Q3W n=120
- Placebo + docetaxel 75 mg/m² Q3W

Primary endpoint:

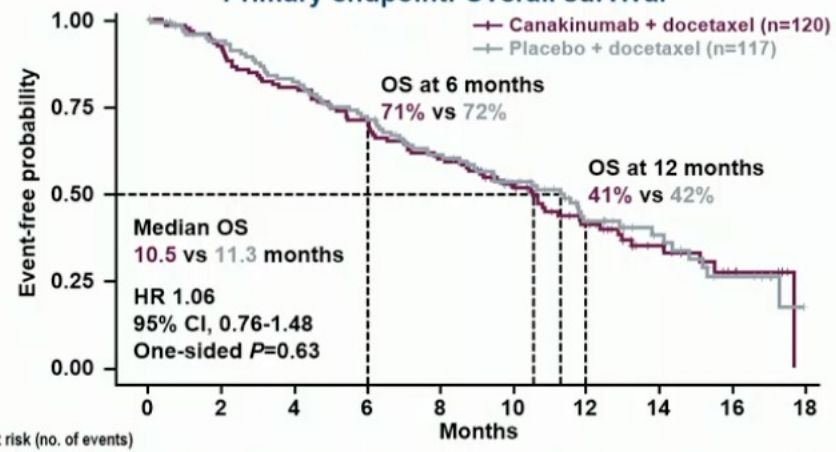
- OS[b]

Secondary endpoints:

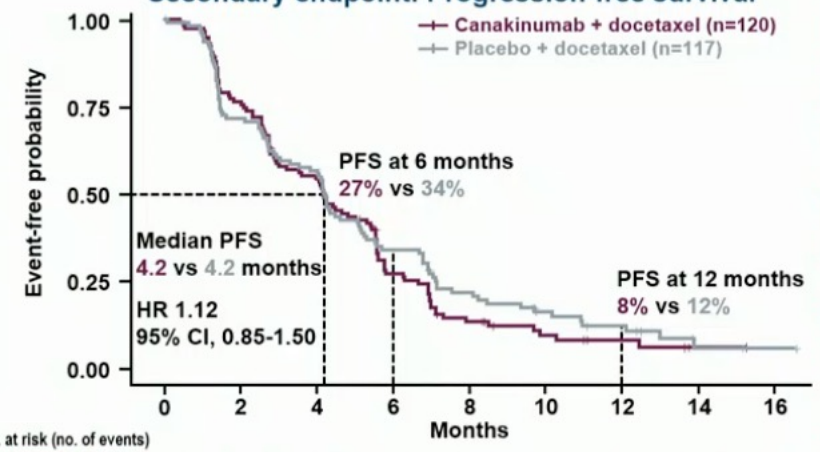
- PFS
- ORR
- DCR
- DOR

Efficacy outcomes

Primary endpoint: Overall survival



Secondary endpoint: Progression-free survival



Paz-Ares et al. ESMO 2021

ESMO 2021: CEACAM-5

Table 1. CEACAM5 expression in whole membrane versus polarized membrane in high and moderate CEACAM5 expressors with NSCLC

	High CEACAM5 expressors (N = 64)[a]		Moderate CEACAM5 expressors (N = 28)	
	Whole membrane	Polarized membrane	Whole membrane	Polarized membrane
Percentage of positive cells with CEACAM5 ≥ 2+ intensity (mean ± SD)	51.95 ± 37.43	25.08 ± 31.69	6.96 ± 9.02	6.89 ± 12.04

[a]N = 63 for polarized membrane.

Scoazec al. ESMO 2021

WCLC 2021: datopotamab deruxtecan

TROPION-PanTumor01 Study Design

Key Inclusion Criteria

- Relapsed/refractory advanced/metastatic NSCLC
- Unselected for TROP2 expression[c]
- Age ≥18 (US) or ≥20 (Japan) years
- ECOG PS 0-1
- Measurable disease per RECIST version 1.1
- Stable, treated brain metastases allowed

Dose Escalation

Dato-DXd 0.27 to 10 mg/kg Q3W[d]

MTD established: 8 mg/kg Q3W

Dose Expansion[b]

NSCLC cohort

- 50 patients at 4 mg/kg
- 50 patients at 6 mg/kg
- 80 patients at 8 mg/kg

TNBC, HR+/HER2−, and other tumor types

Primary objectives

- Establish MTD; safety, tolerability

Secondary objectives[e]

- Efficacy,[f] PK, ADAs

6-mg/kg dose chosen for further development[6,7]

Antitumor Activity of Dato-DXd

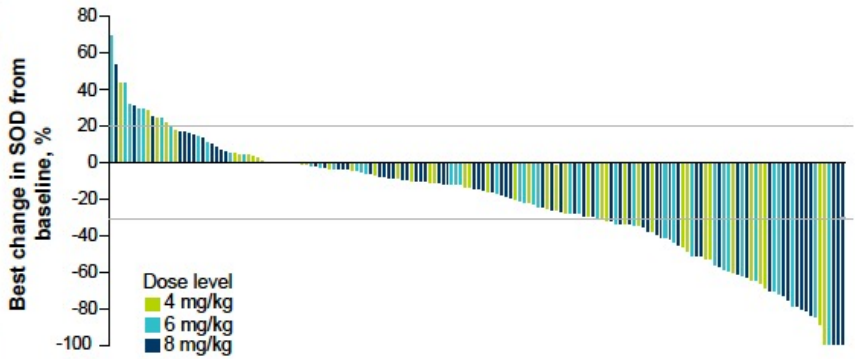
Best Overall Response (BICR)

Patients[a]	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)[b]	12 (24)	14 (28)	19 (24)
CR, n (%)	0	0	1 (1)
PR, n (%)[b]	12 (24)	14 (28)	18 (23)
SD, n (%)	25 (50)	20 (40)	42 (53)
Non-CR/PD, n (%)	1 (2)	2 (4)	2 (3)
PD, n (%)	7 (14)	10 (20)	8 (10)
NE, n (%)	5 (10)	5 (10)	9 (11)
DOR, median (95% CI), mo	NE (2.8-NE)	10.5 (5.6-NE)	9.4 (5.8-NE)

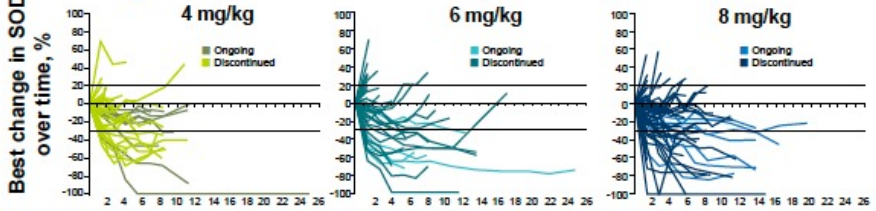
- Antitumor activity was observed at 4-, 6-, and 8-mg/kg doses of Dato-DXd
- Most responses were durable over time, including a median duration of response of 10.5 months in the 6-mg/kg cohort

Data cutoff: April 6, 2021.

Best Change in Sum of Diameters (per BICR)



Change in Sum of Diameters of Target Lesion (per BICR) Over Time



Garon al. WCLC 2021

Les cancers thoraciques

Non à petites cellules

- Stades précoces
- Dépistage
- Localement avancés
  - Résécables
  - Non résécables
- Métastatiques
  - Oncogène addictif
  - Sans oncogène addictif

Petites cellules

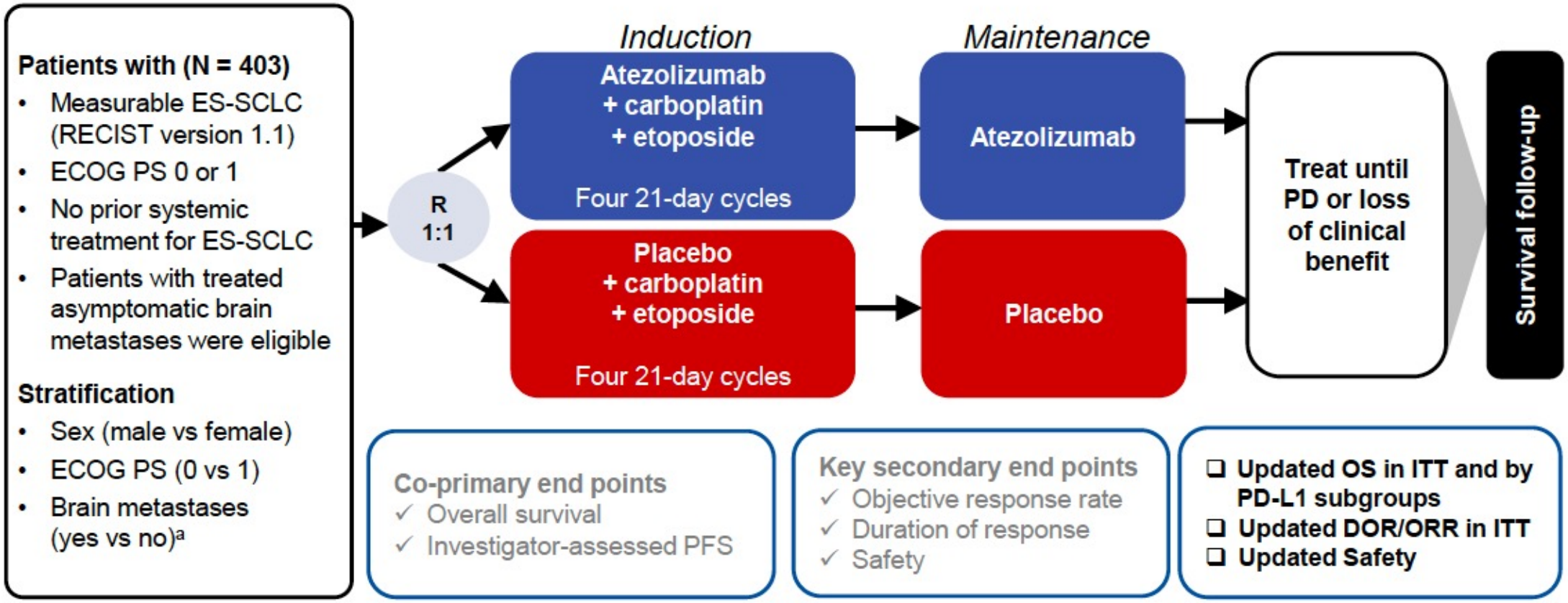
- Localement avancés
- **Métastatiques**

Mésothéliome

Tumeurs thymiques

Cancers bronchiques à petites cellules métastatiques
Chimiothérapie et immunothérapie

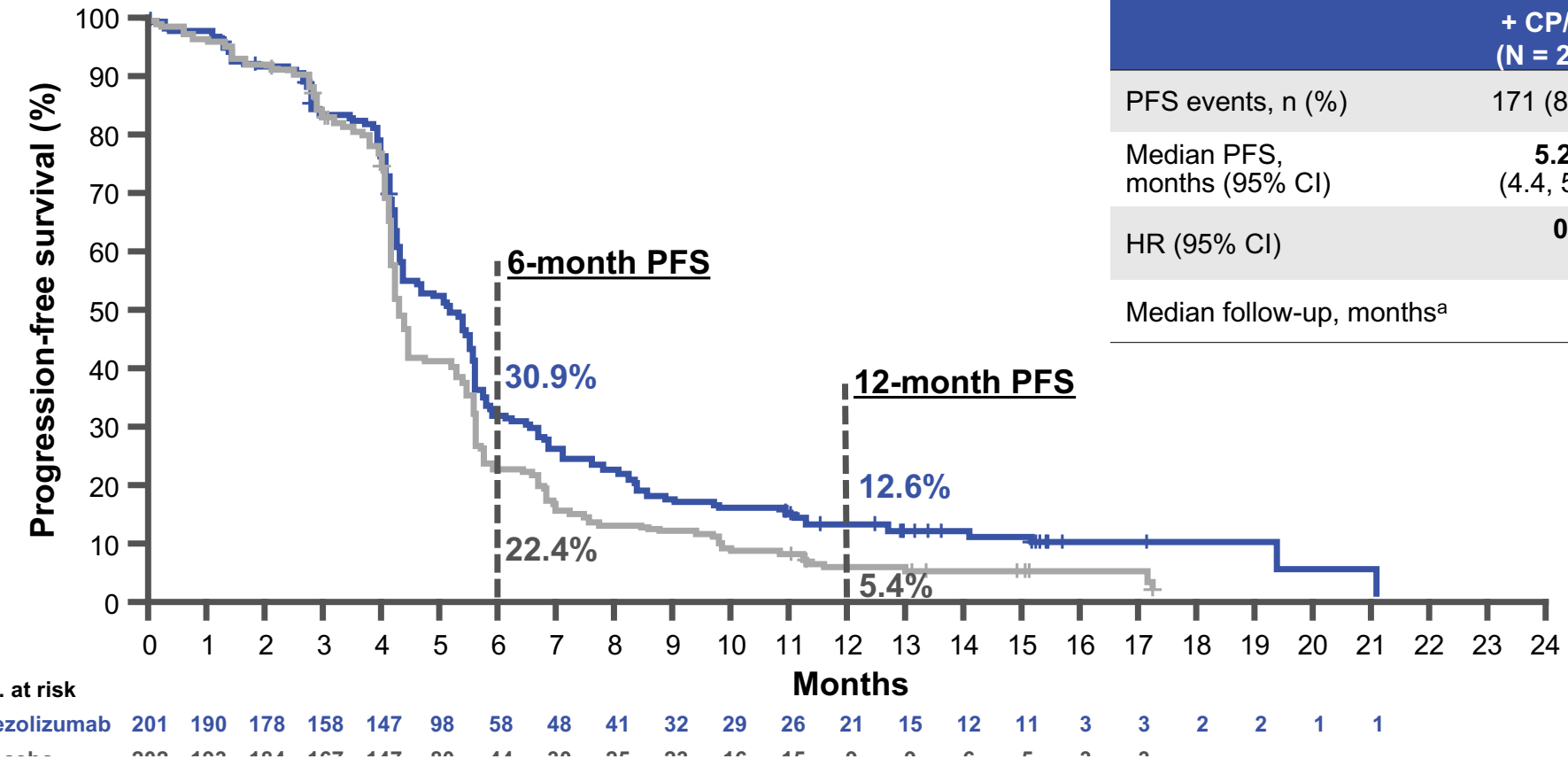
IMPOWER-133



Reck et al. ESMO 2019

Cancers bronchiques à petites cellules métastatiques
Chimiothérapie et immunothérapie

IMPOWER-133



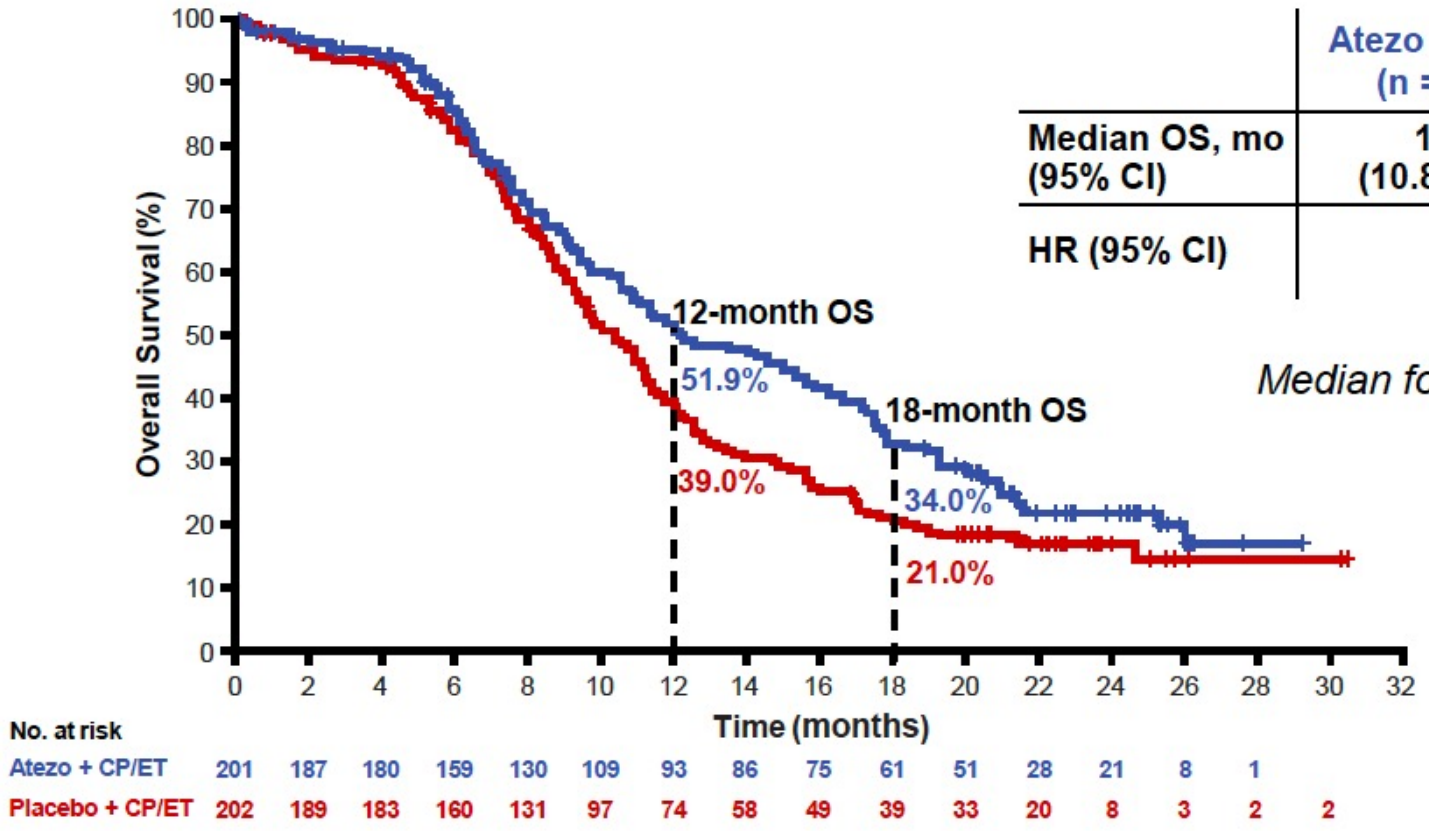
	Atezolizumab + CP/ET (N = 201)	Placebo + CP/ET (N = 202)
PFS events, n (%)	171 (85.1)	189 (93.6)
Median PFS, months (95% CI)	**5.2** (4.4, 5.6)	**4.3** (4.2, 4.5)
HR (95% CI)	**0.77** (0.62, 0.96) p = 0.017	
Median follow-up, months[a]	13.9	

Paz-Ares et al. WCLC 2018

Cancers bronchiques à petites cellules métastatiques
Chimiothérapie et immunothérapie

IMPOWER-133

Updated OS in ITT



	Atezo + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8, 15.8)	10.3 (9.3, 11.3)
HR (95% CI)	0.76 (0.60, 0.95) p = 0.0154[a]	

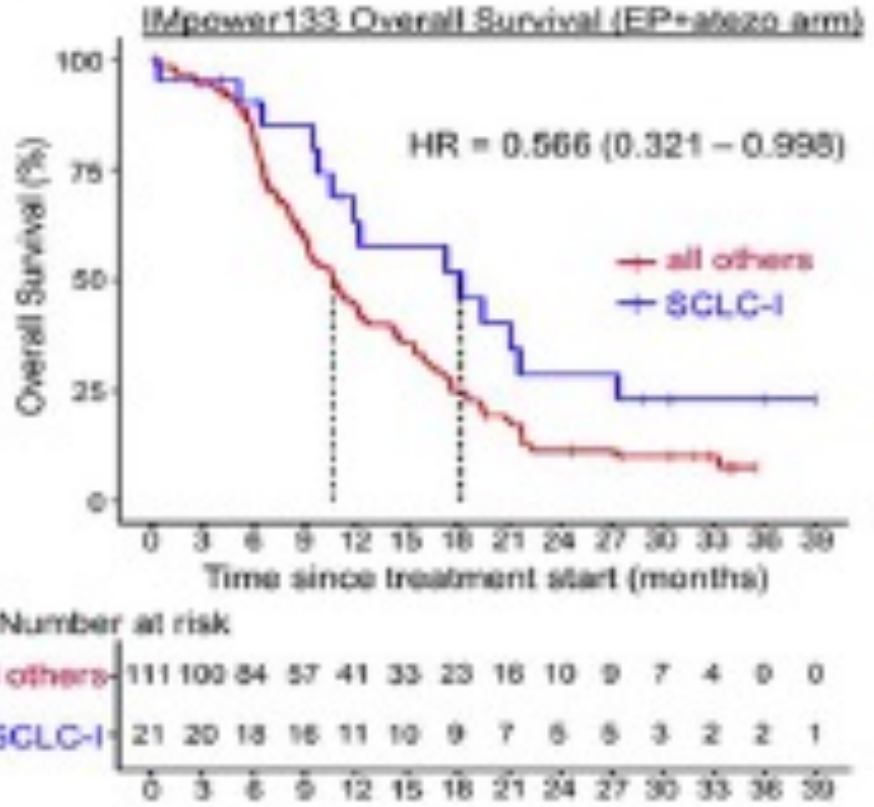
Median follow-up, 22.9 months

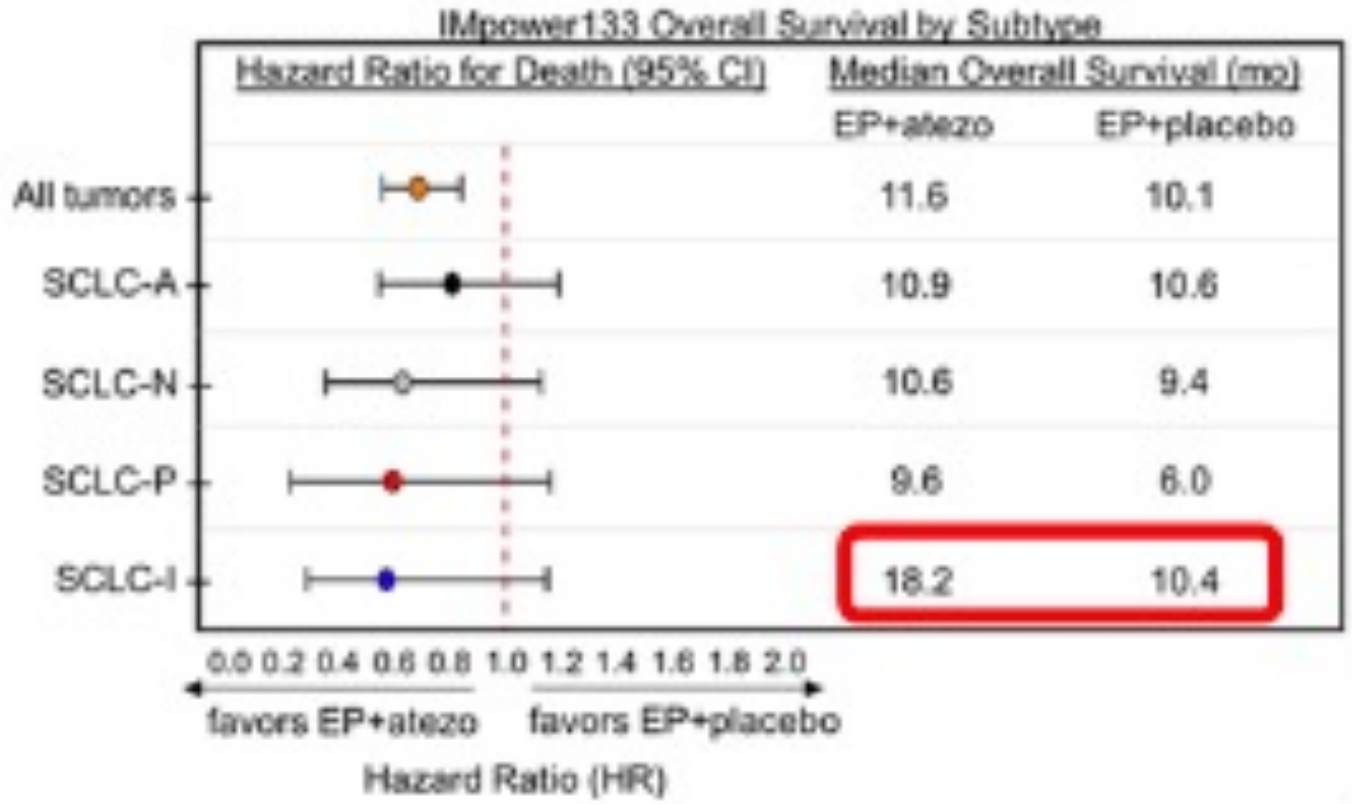
[a]p-value is provided for descriptive purpose.
CCOD 24 January 2019

Reck et al. ESMO 2019

Cancers bronchiques à petites cellules métastatiques
Chimiothérapie et immunothérapie

IMPOWER-133

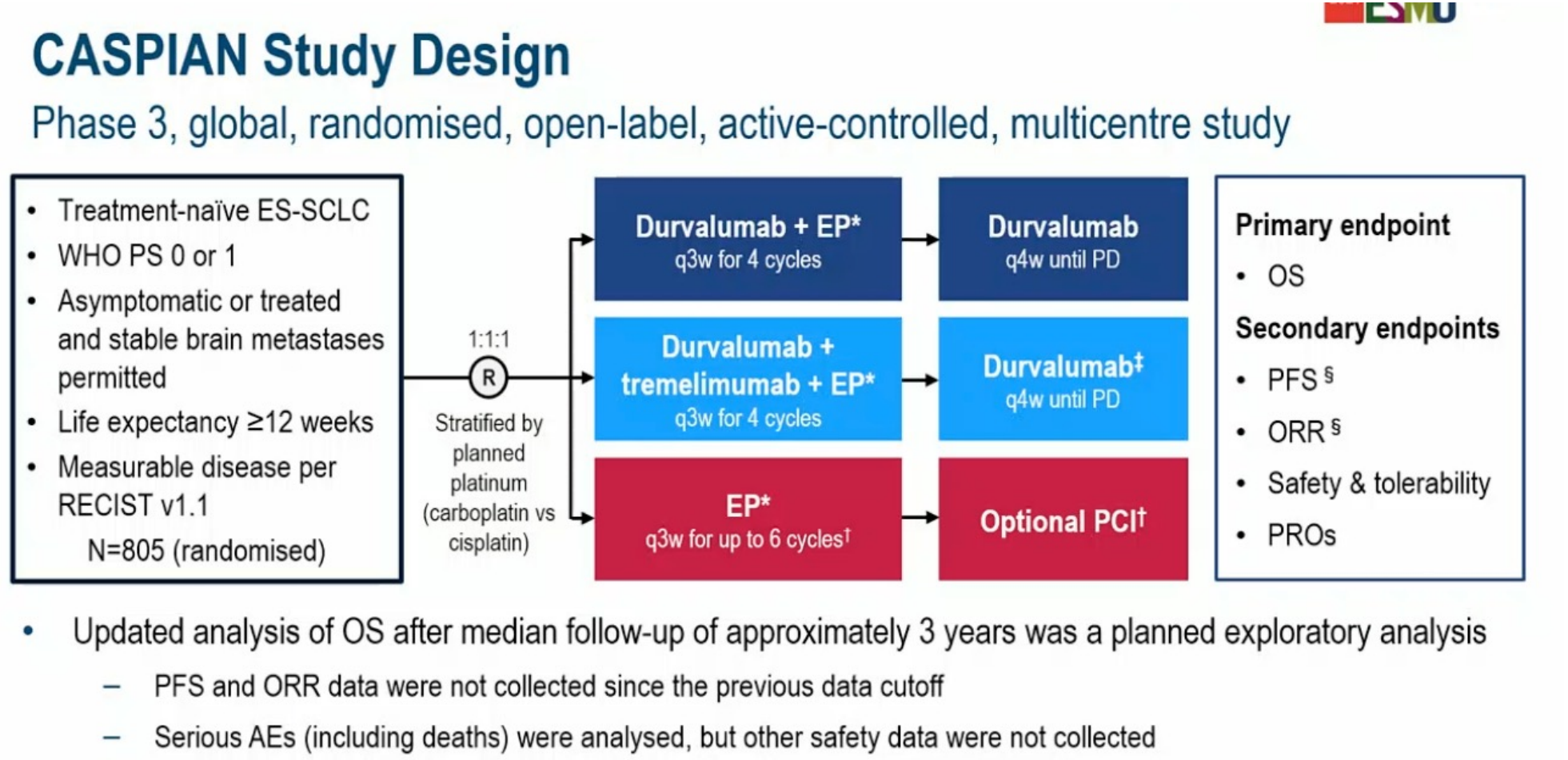




Horn et al. NEJM 20218

Small cell lung cancer
Immunotherapy with chemotherapy

CASPIAN Study Design

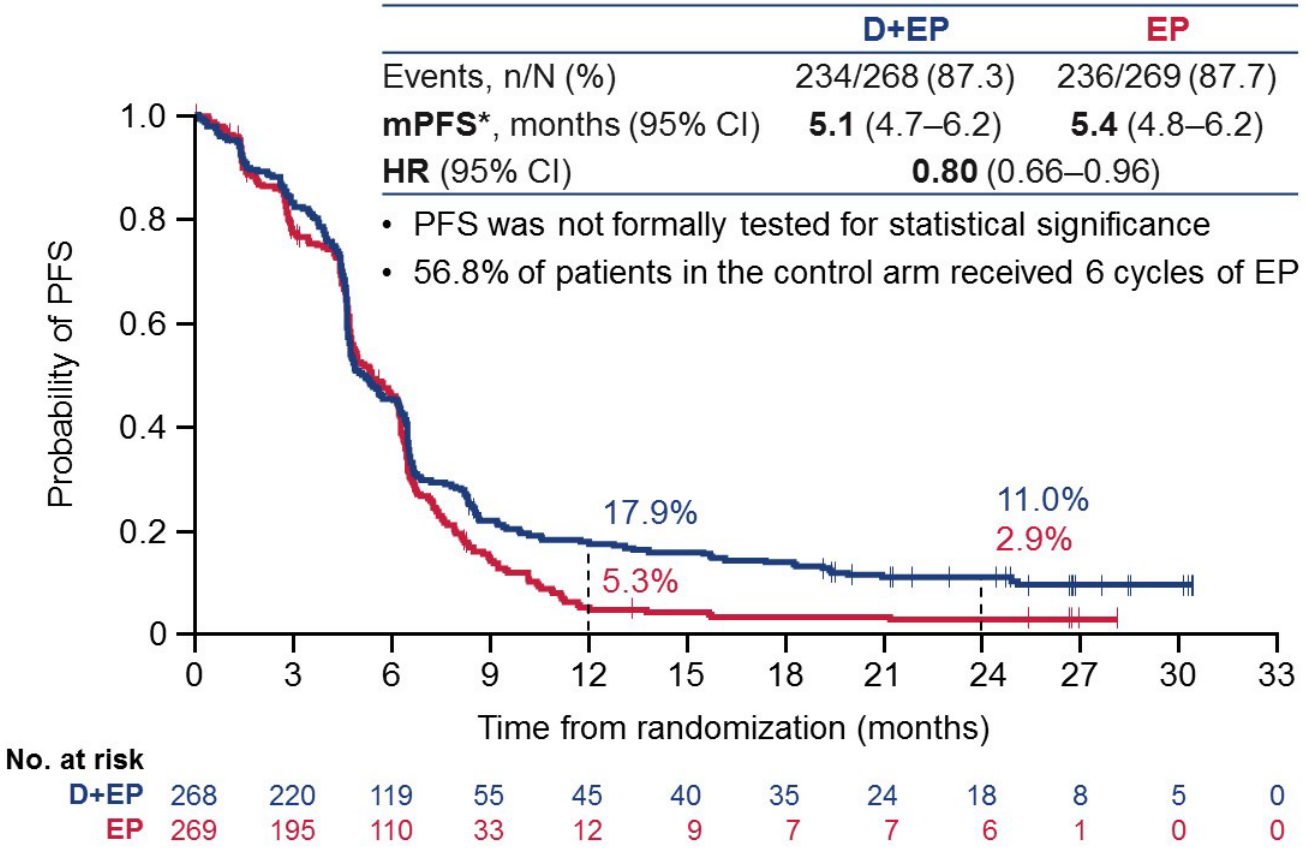


Paz-Ares et al. ESMO 2021

Cancers bronchiques à petites cellules métastatiques
Chimiothérapie et immunothérapie

CASPIAN

Updated Progression-free Survival: D+EP vs EP

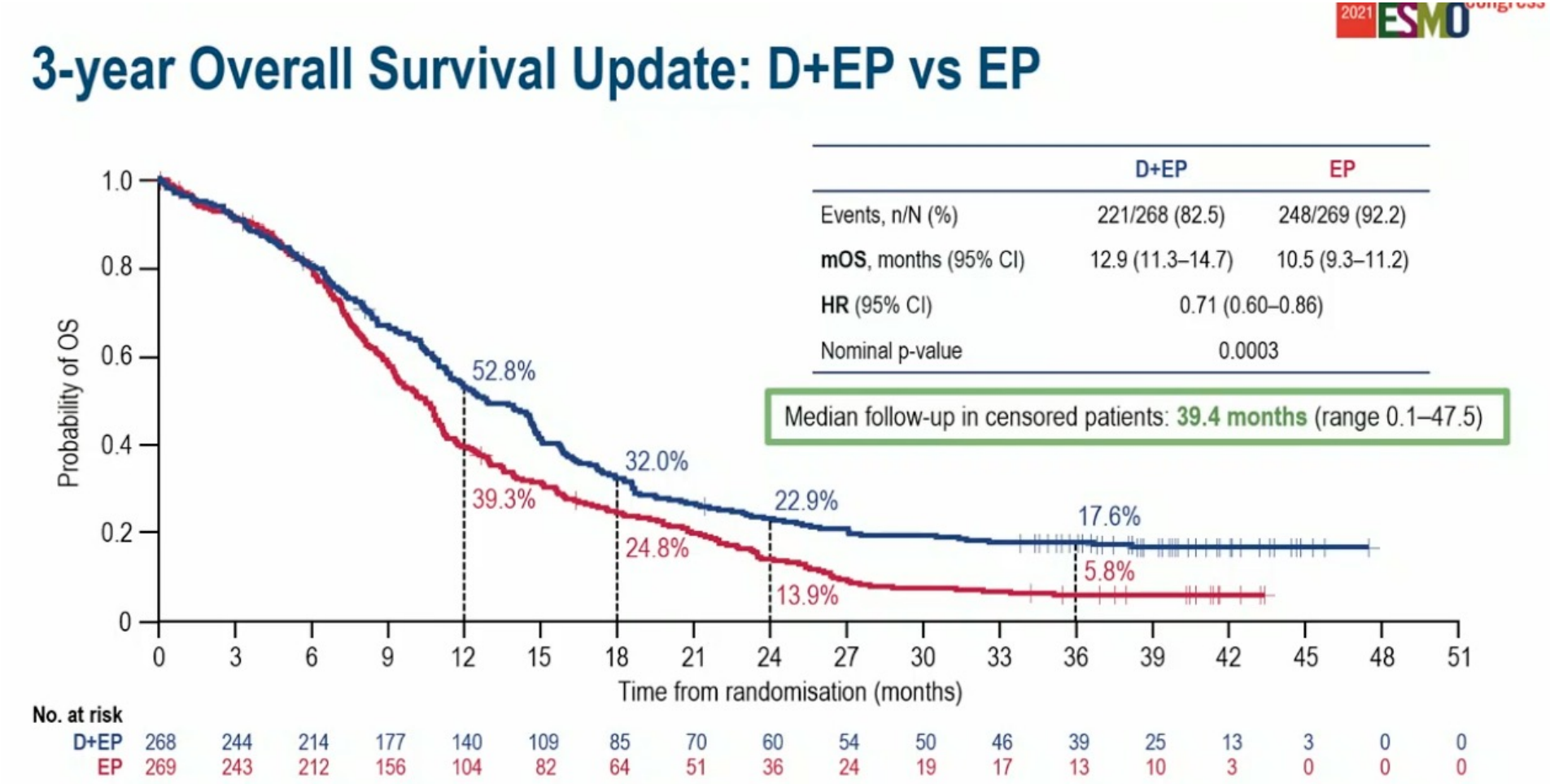


Landmark PFS, %	D+EP (n=268)	EP (n=269)
6 months	45.4	45.8
12 months	17.9	5.3
18 months	13.9	3.4
24 months	11.0	2.9

Paz-Ares et al. ASCO 2020

Cancers bronchiques à petites cellules métastatiques
Chimiothérapie et immunothérapie

CASPIAN



Paz-Ares et al. ESMO 2021

Les cancers thoraciques

Non à petites cellules

- Stades précoces
- Dépistage
- Localement avancés
  - Résécables
  - Non résécables
- Métastatiques
  - Oncogène addictif
  - Sans oncogène addictif

Petites cellules

- Localement avancés
- **Métastatiques**

Mésothéliome

Tumeurs thymiques

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

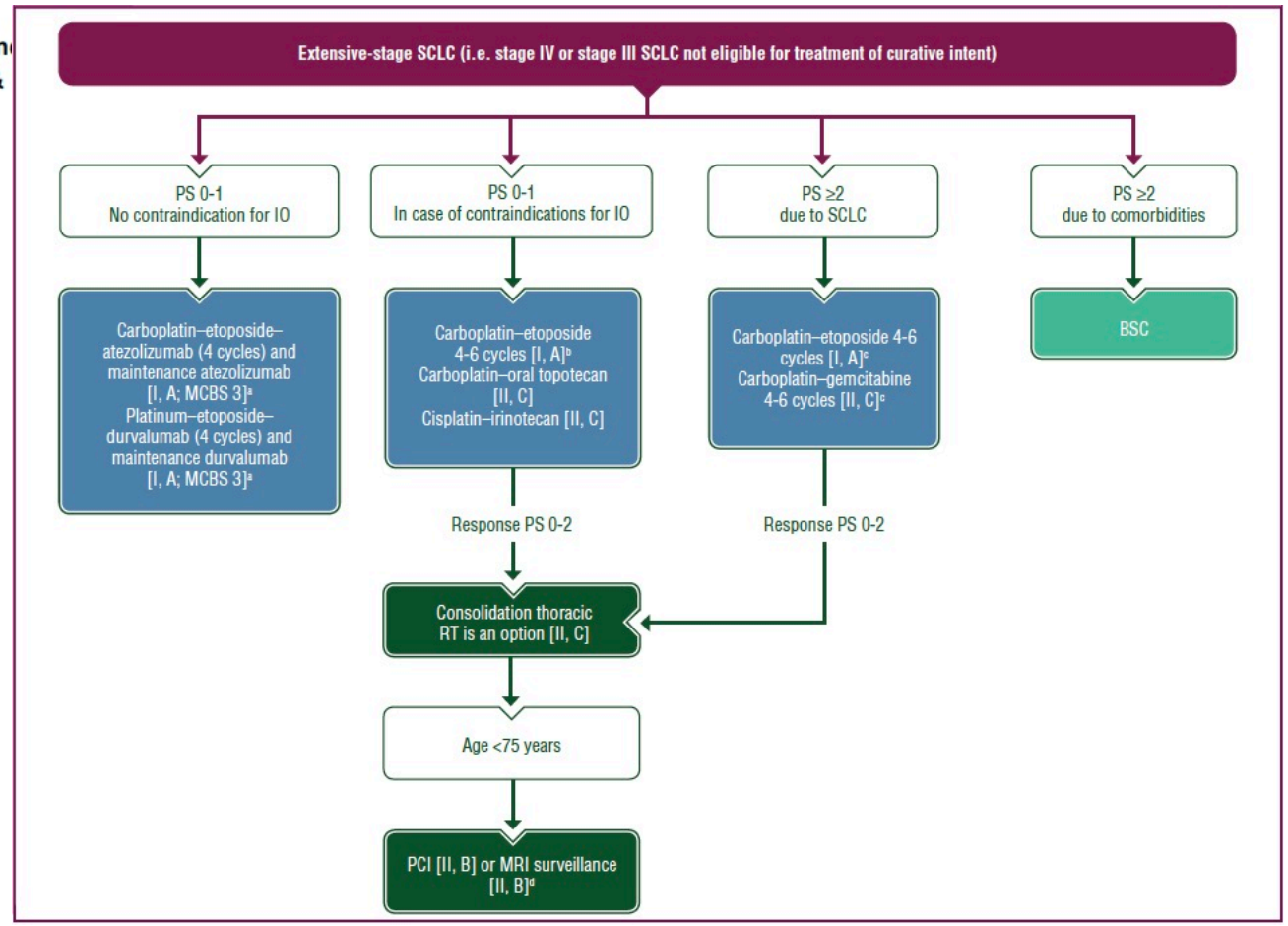
SPECIAL ARTICLE

Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up☆

A.-M. C. Dingemans[1,2], M. Früh[3,4], A. Ardizzoni[5], B. Besse[6,7], C. Faivre-Finn[8], L. E. Hen
N. Reguart[11], C. M. Rudin[12], D. De Ruysscher[13], P. E. Van Schil[14], J. Vansteenkiste[15] &
Guidelines Committee*

Table 1. Diagnostic and staging work-up of SCLC

History and clinical examination
Medical history (including smoking history and comorbidities)
PS
Physical examination
Assessment of paraneoplastic syndromes (especially when initiating immunotherapy)
Laboratory analysis
CBC, liver enzymes, sodium, potassium, calcium, glucose, LDH and renal functions tests should be carried out
Imaging
CT of the thorax and abdomen should be carried out in all patients; an FDG—PET—CT is optional
In case of a suspicion of bone metastasis and no other metastasis, a bone scintigraphy should be carried out unless FDG—PET is available
Imaging of the brain (preferably MRI) is mandated in patients with stage I-III disease
MRI of the brain is recommended for patients with stage IV disease who are eligible for PCI but who choose not to undergo PCI
Tumour biopsy
A diagnosis of SCLC is preferably assessed based on histological examination of a biopsy
In case of planned surgery, invasive mediastinal staging is required
Functional assessment
Pulmonary function testing (FEV1, VC, DLCO) is required for patients with stage I-III SCLC who are candidates for surgery or RT
VO2 max assessment by cycle ergometry should be carried out if surgery is planned when pulmonary function tests are limited



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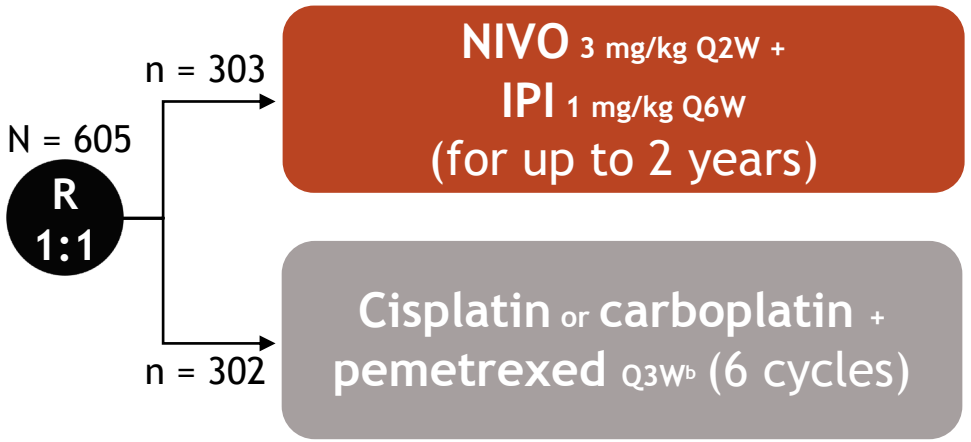
Mésothéliome

Tumeurs thymiques

Mésothelioma: First-line immunotherapy as a standard CheckMate-743

Key eligibility criteria
- Unresectable MPM
- No prior systemic therapy
- ECOG PS 0–1

Stratified by
Histology (epithelioid vs non-epithelioid) and gender



Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

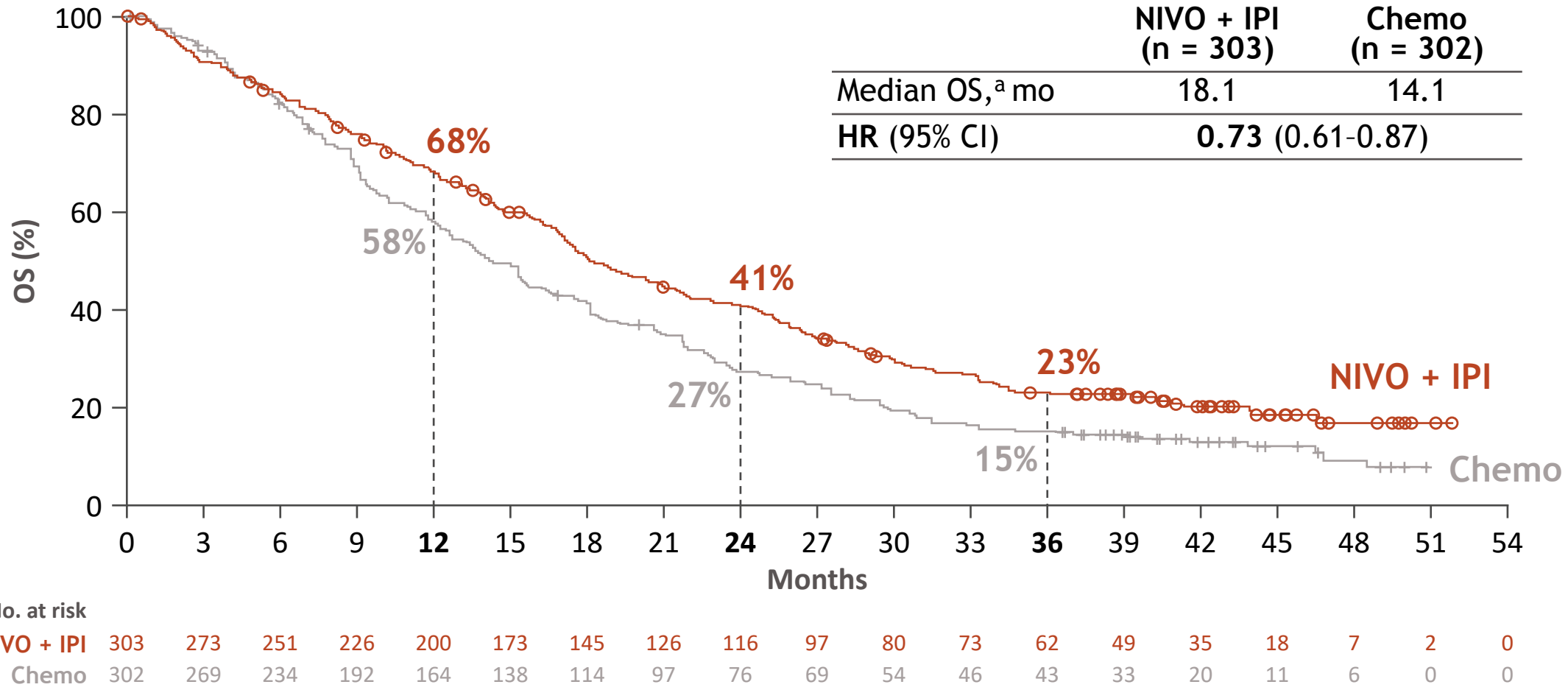
Primary endpoint
- OS

Secondary endpoints
- ORR, DCR, and PFS by BICR
- Efficacy by PD-L1[c] expression

Exploratory endpoints
- Safety and tolerability
- Biomarkers

Peters et al. ESMO 2021

Mésothelioma: First-line immunotherapy as a standard CheckMate-743

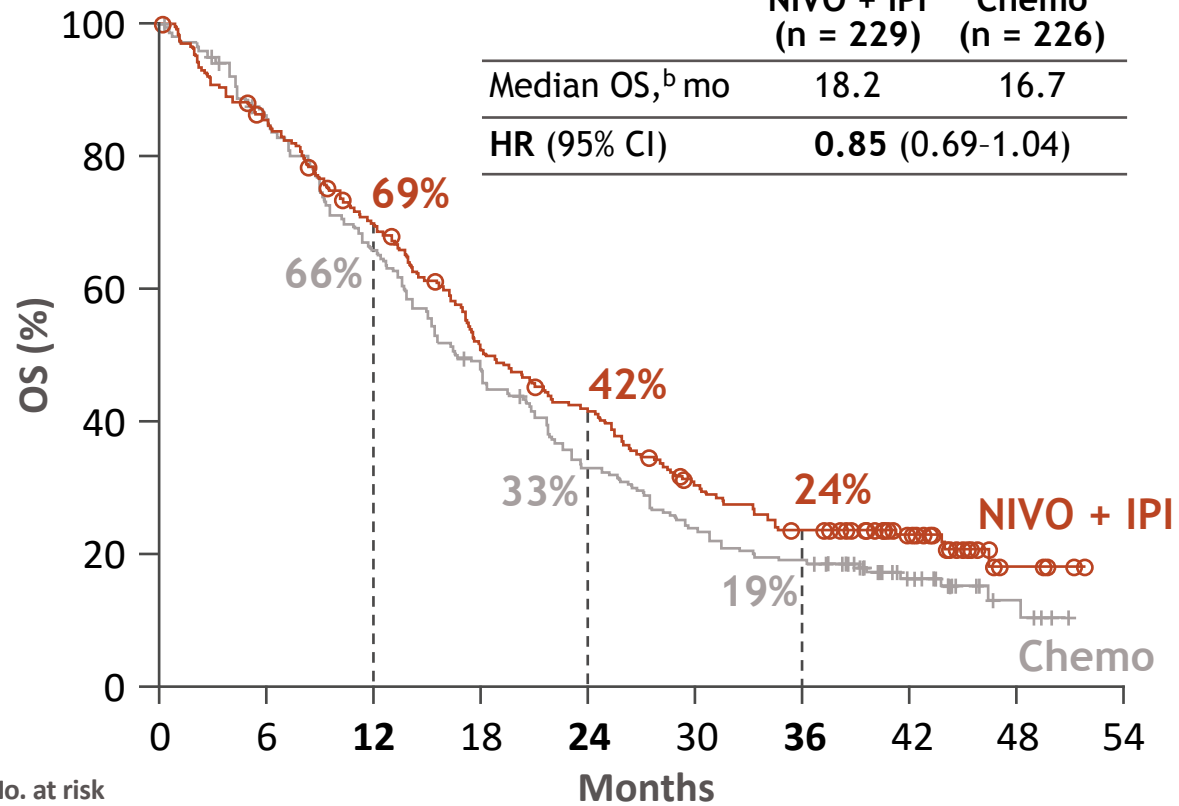


Peters et al. ESMO 2021

Mésothelioma: First-line immunotherapy as a standard CheckMate-743

Epithelioid

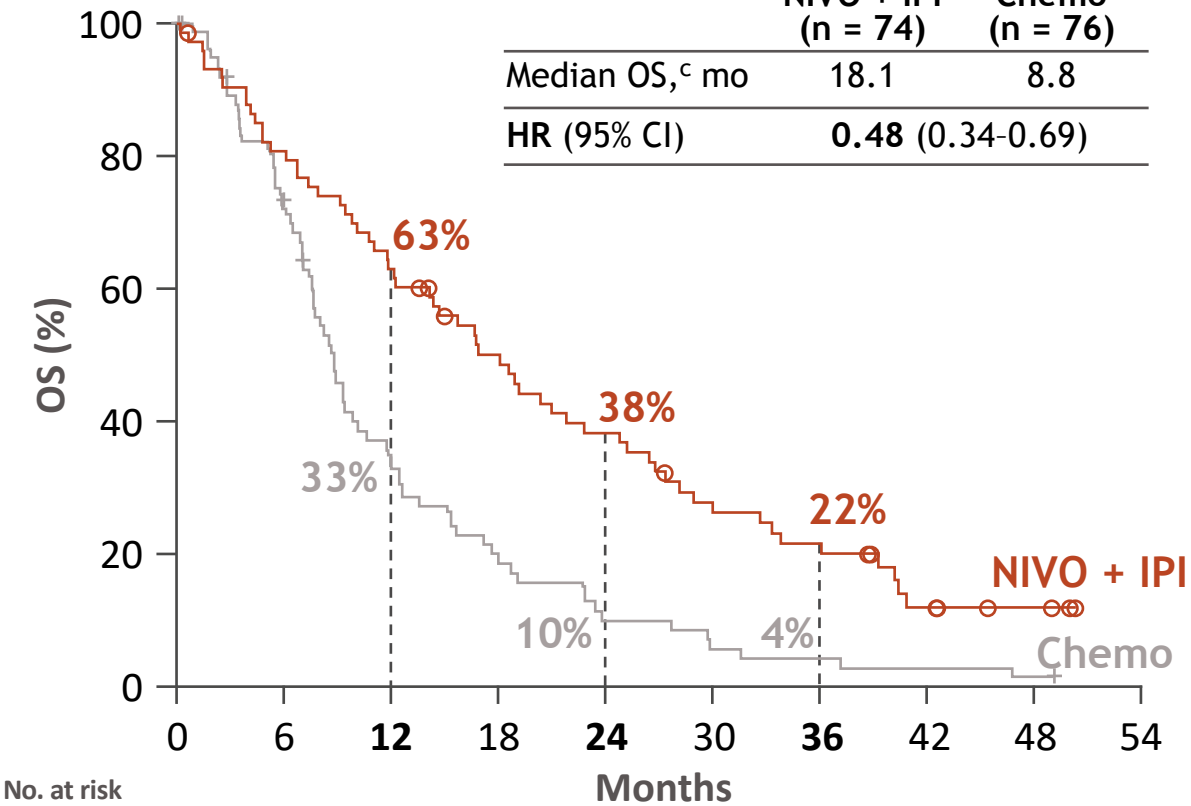
	NIVO + IPI (n = 229)	Chemo (n = 226)
Median OS,[b] mo	18.2	16.7
HR (95% CI)	**0.85** (0.69-1.04)	



No. at risk										
NIVO + IPI	229	192	154	111	90	63	48	29	4	0
Chemo	226	182	141	101	69	50	40	18	5	0

Non-epithelioid

	NIVO + IPI (n = 74)	Chemo (n = 76)
Median OS,[c] mo	18.1	8.8
HR (95% CI)	**0.48** (0.34-0.69)	



No. at risk										
NIVO + IPI	74	59	46	34	26	17	14	6	3	0
Chemo	76	52	23	13	7	4	3	2	1	0

Peters et al. ESMO 2021

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Mésothéliome

Tumeurs thymiques

Merci!

Institut du thorax Curie - Montsouris

Inserm
La science pour la santé
From science to health

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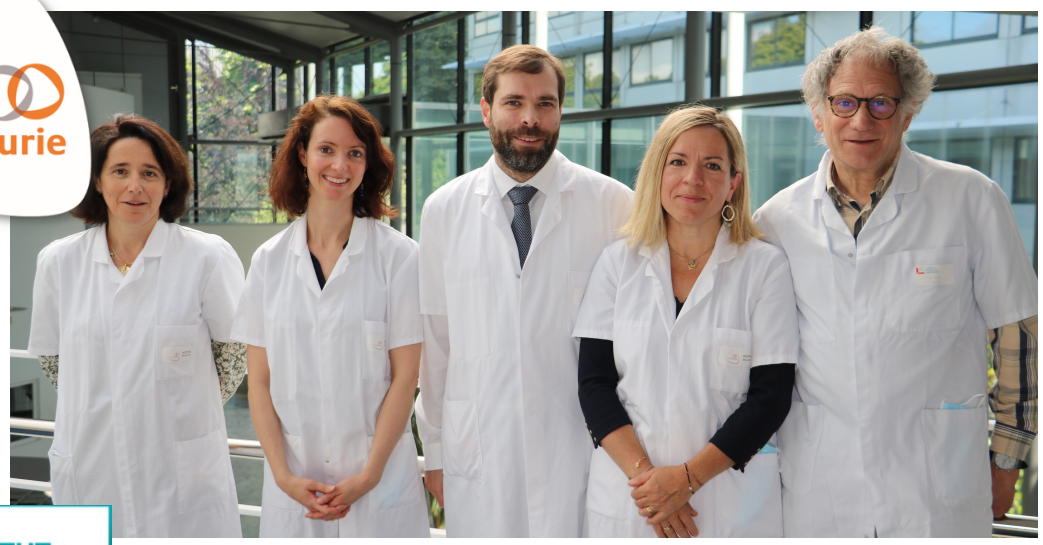

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