Immunoterapia per tutti?
Come cambia l'algoritmo terapeutico

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Disclosures

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Speaker fees: MSD, Astrazeneca, Astellas

Commissioned publishing: Ipsen, Roche

Opening statement

In 20 minuti non riusciremo mai a discutere dell'immunoterapia nel:

NSCLC Stadio IV, I e II linea

NSCLC Stadio III

NSCLC Neo/Adiuvante

SCLC I e II linea

(Per fortuna) all'ultimo ASCO non sono stati presentati ulteriori dati practice changing!

Agenda

- SCLC, first line
- NSCLC stage III
- NSCLC stage IV, first line (wild type)
- NSCLC stage IV, oncogene addicted
- What we've learned from IO-clinical practice
- Conclusions

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- **NSCLC stage IV, first line (wild type)**
- NSCLC stage IV, oncogene addicted
- What we've learned from IO-clinical practice
- Conclusions

Keynote-024: Pembrolizumab vs chemotherapy in PD-L1 ≥ 50%

Key Eligibility Criteria

- Untreated stage IV NS
- PD-L1 TPS ≥50%
- ECOG PS 0-1
- No activating *EGFR* m
  ALK translocation
- No untreated brain me
- No active autoimmune
  requiring systemic the

Pembrolizumab

Key End Points

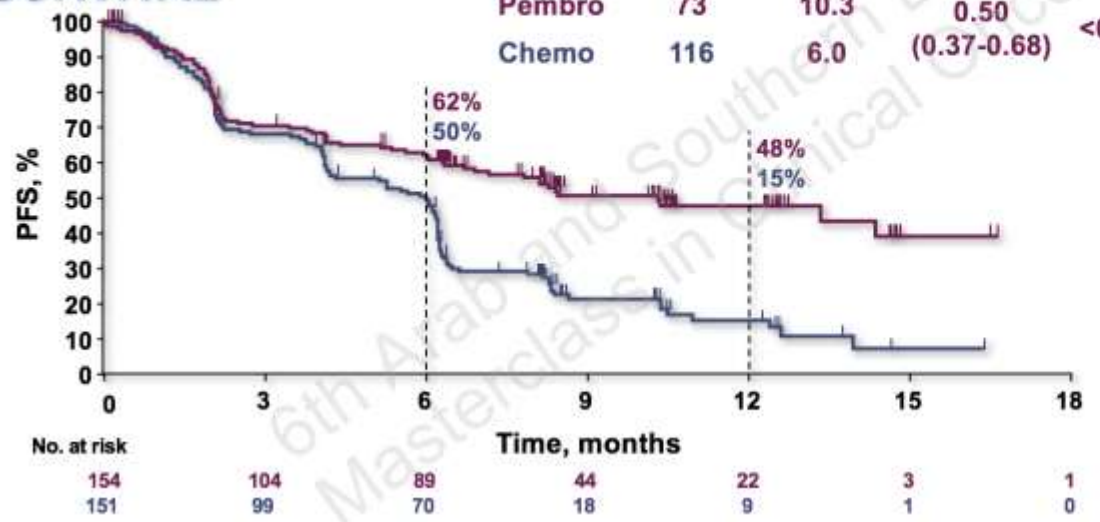
Primary: PFS (RECI

Secondary: OS, ORR, safety

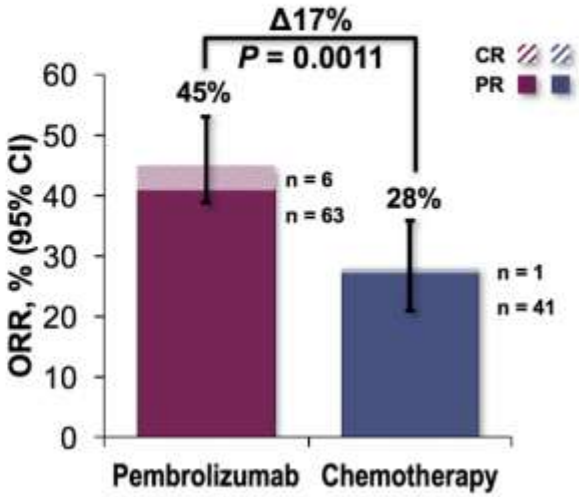
Exploratory: DOR

PROGRESSION-FREE SURVIVAL

	Events, n	Median, mo	HR (95% CI)	P
Pembro	73	10.3	0.50 (0.37-0.68)	<0.001
Chemo	116	6.0		

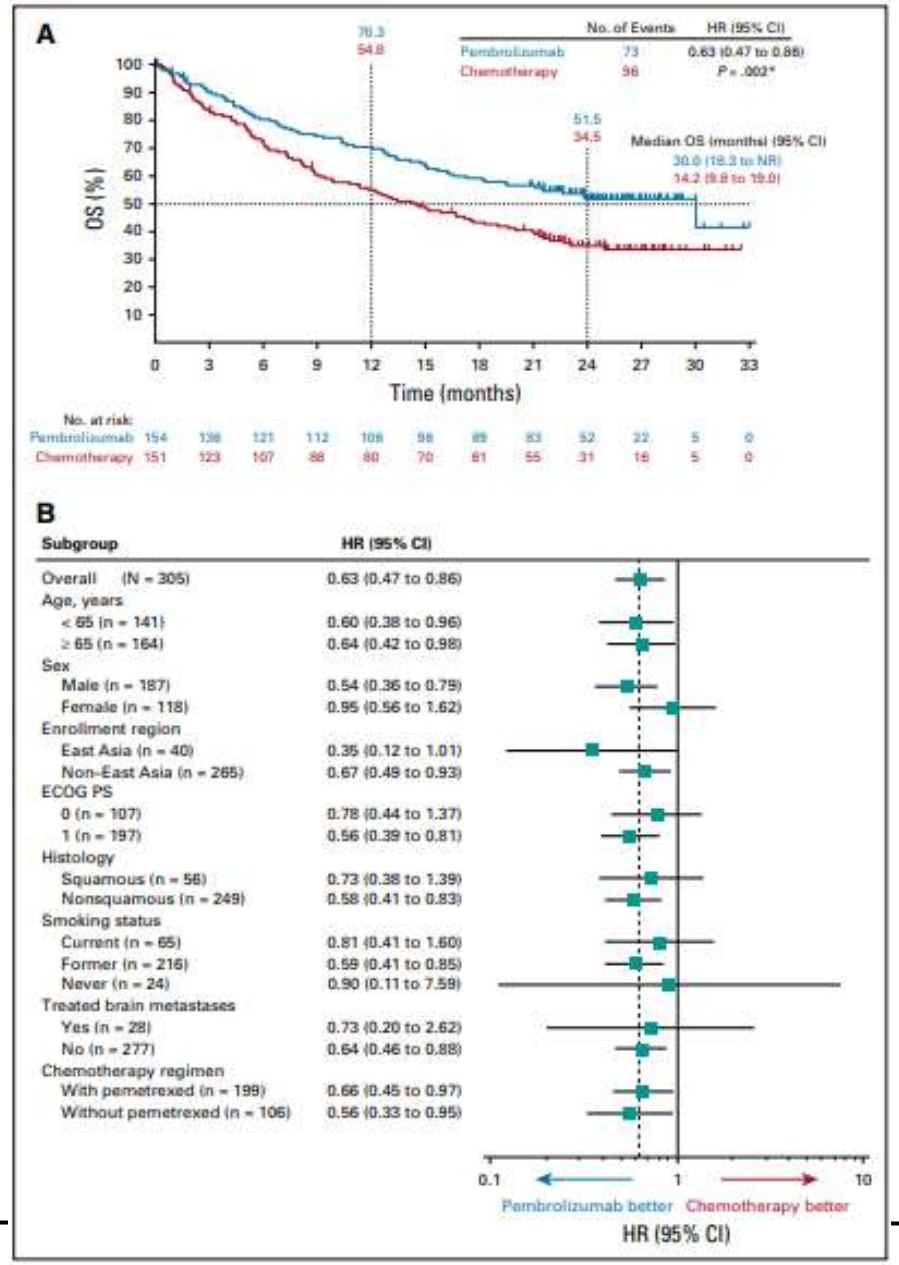


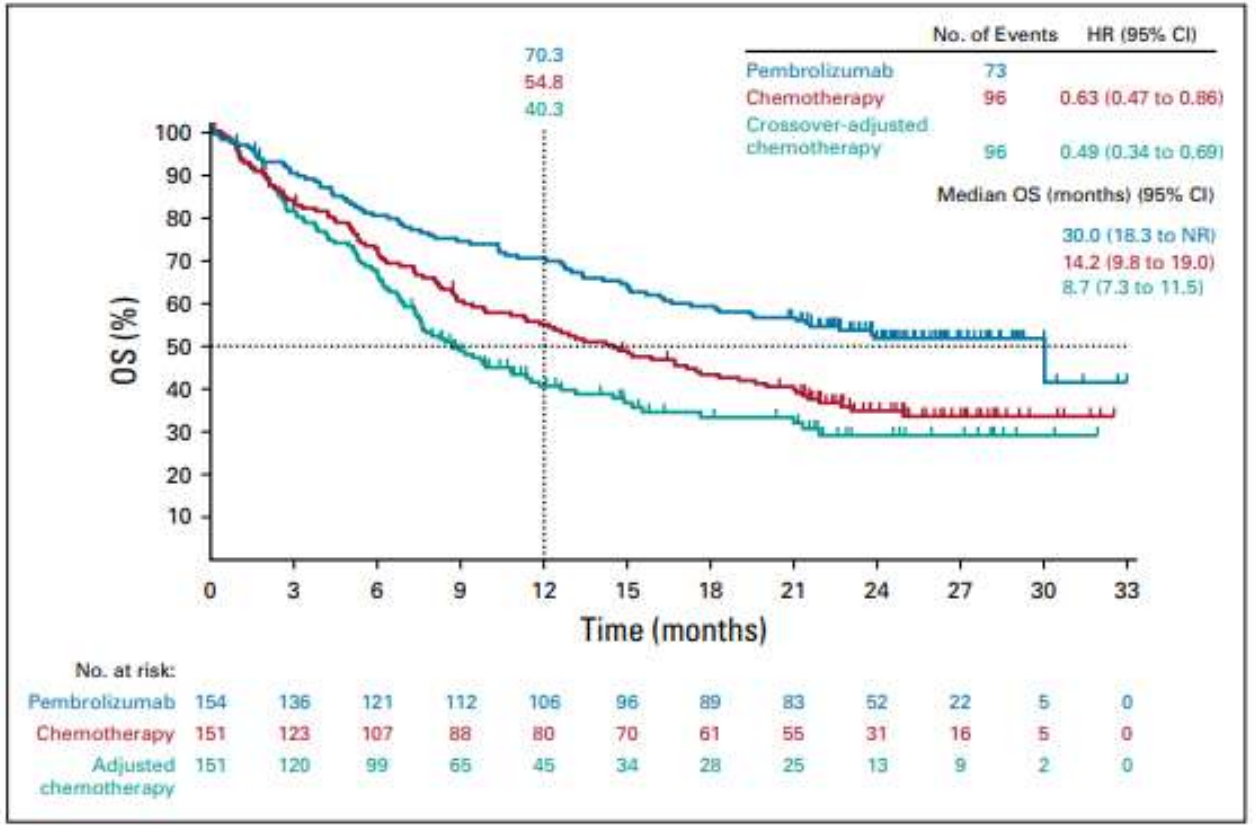
OBJECTIVE RESPONSE



Reck M, et al NEJM 2016

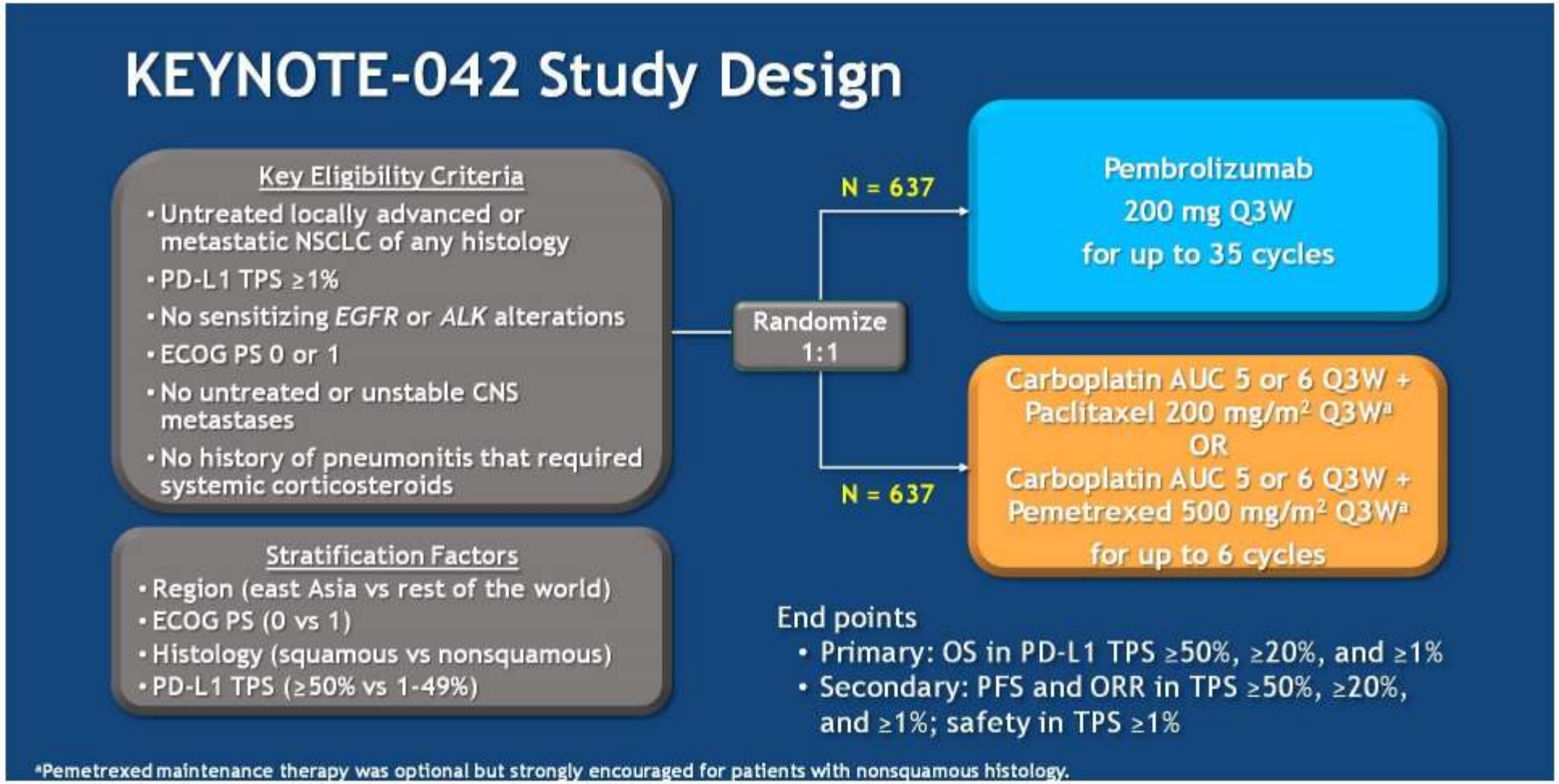
Keynote-024: 2-Years OS update





Reck M, et al. JCO 2019

Keynote-042: Pembrolizumab vs chemotherapy in PD-L1 ≥ 1%

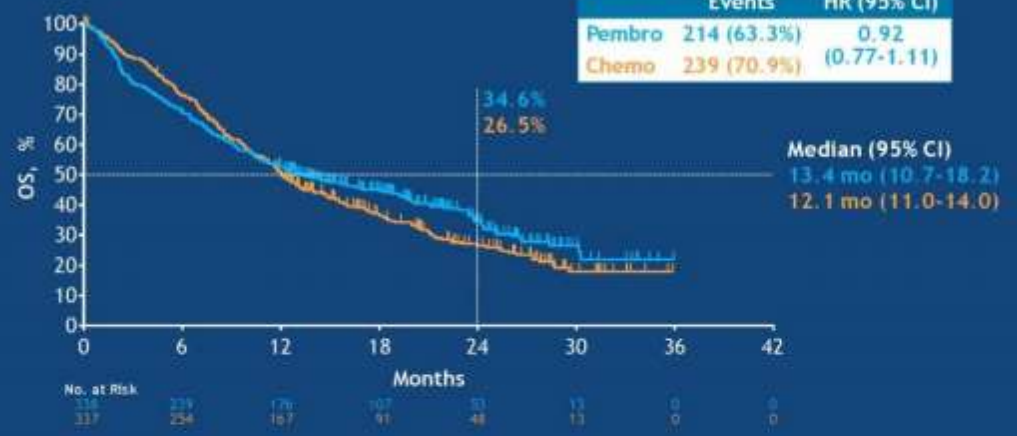


Lopes G, ASCO 2018

Keynote-042: Pembrolizumab vs chemotherapy in PD-L1 ≥ 1%

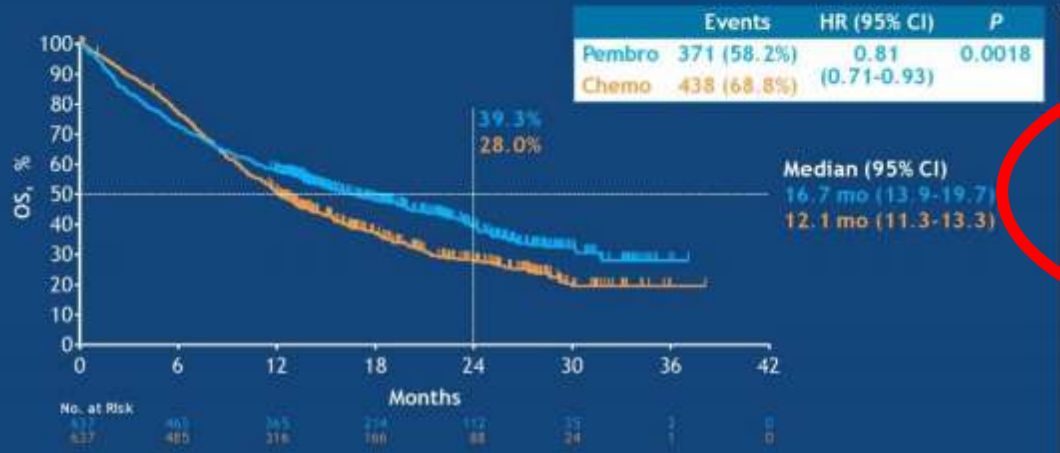
Overall Survival: TPS ≥50%

Overall Survival: TPS ≥1-49% (Exploratory Analysis[a])



[a]No alpha allocated to this comparison.

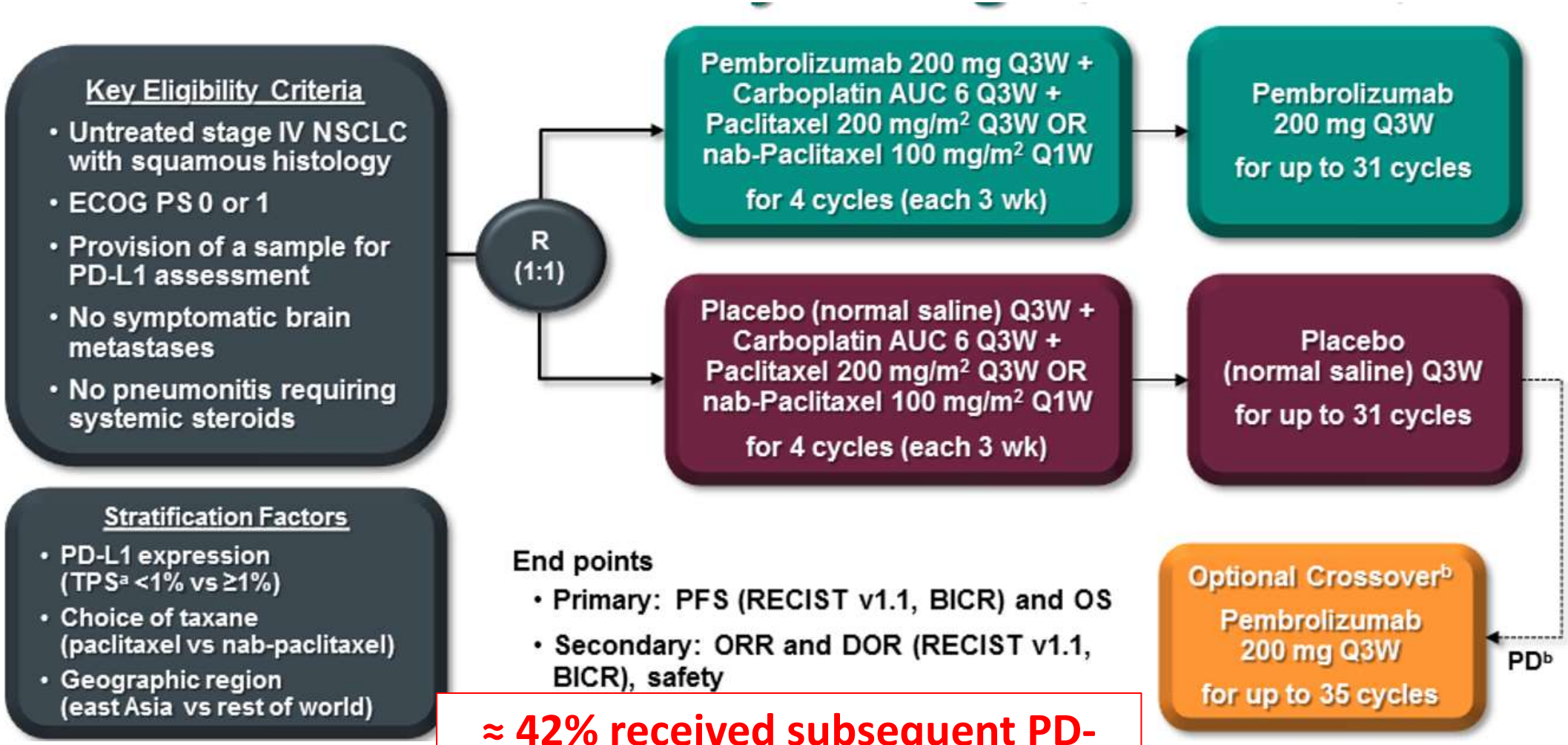
Overall Survival: TPS ≥1%



- **Cross-over not permitted**
- **47% of PD-L1 ≥ 50%**

Lopes G, ASCO 2018; Mok T, et al. Lancet 2019

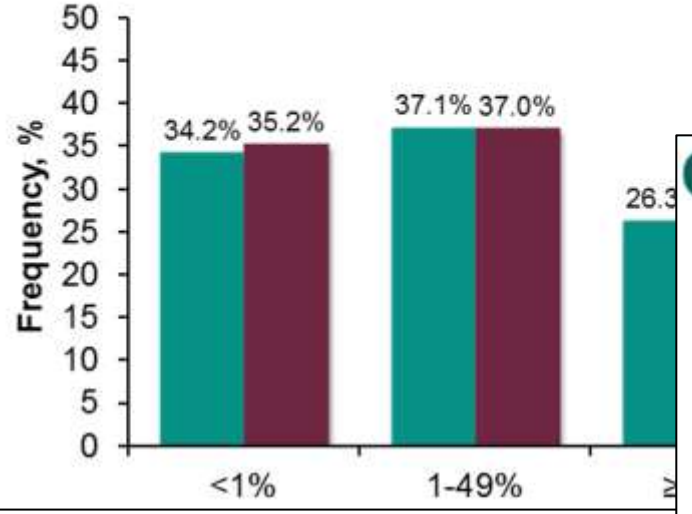
Keynote-407: Pembrolizumab +/- chemotherapy in Sq-NSCLC



≈ 42% received subsequent PD-1/PD-L1 inhibitors

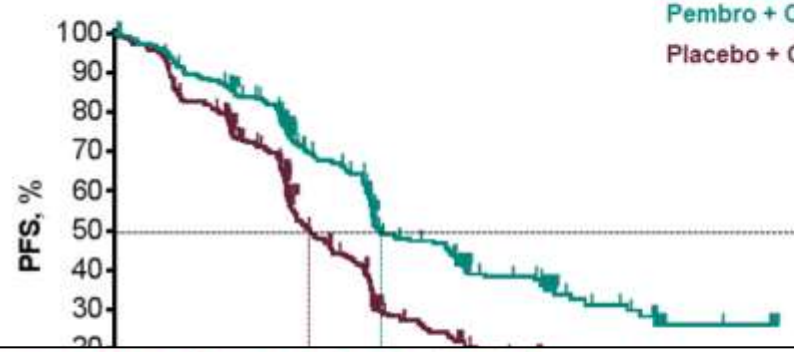
Keynote-407: Pembrolizumab +/- chemotherapy in Sq-NSCLC

Frequency of PD-L1 TPS Categ



Progression-Free Survival at IA2, ITT

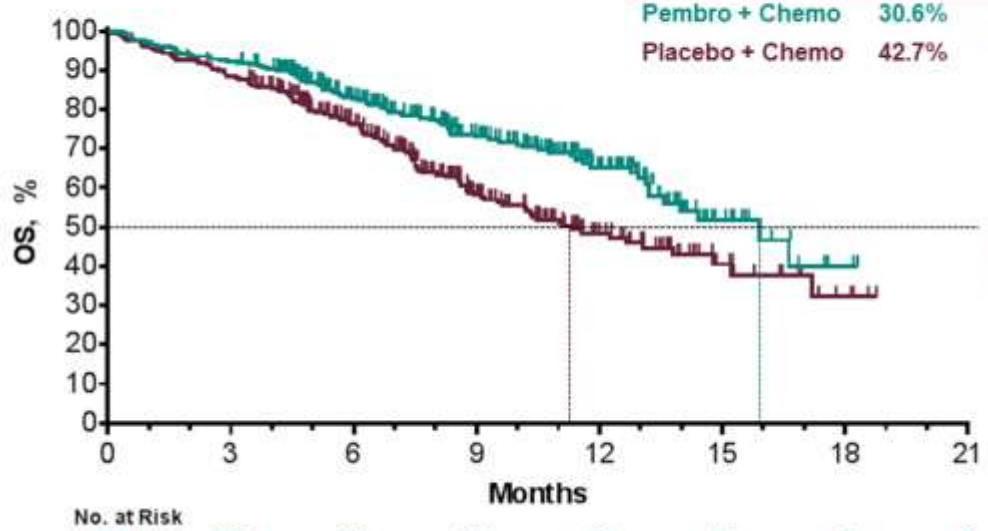
	Events	HR (95% CI)	P
Pembro + Chemo	54.7%	0.56 (0.45-0.70)	<0.0001
Placebo + Chemo	70.1%		



Median (95% CI)
6.4 mo (6.2-8.3)
4.8 mo (4.3-5.7)

Overall Survival at IA2, ITT

	Events	HR (95% CI)	P
Pembro + Chemo	30.6%	0.64 (0.49-0.85)	0.0008
Placebo + Chemo	42.7%		

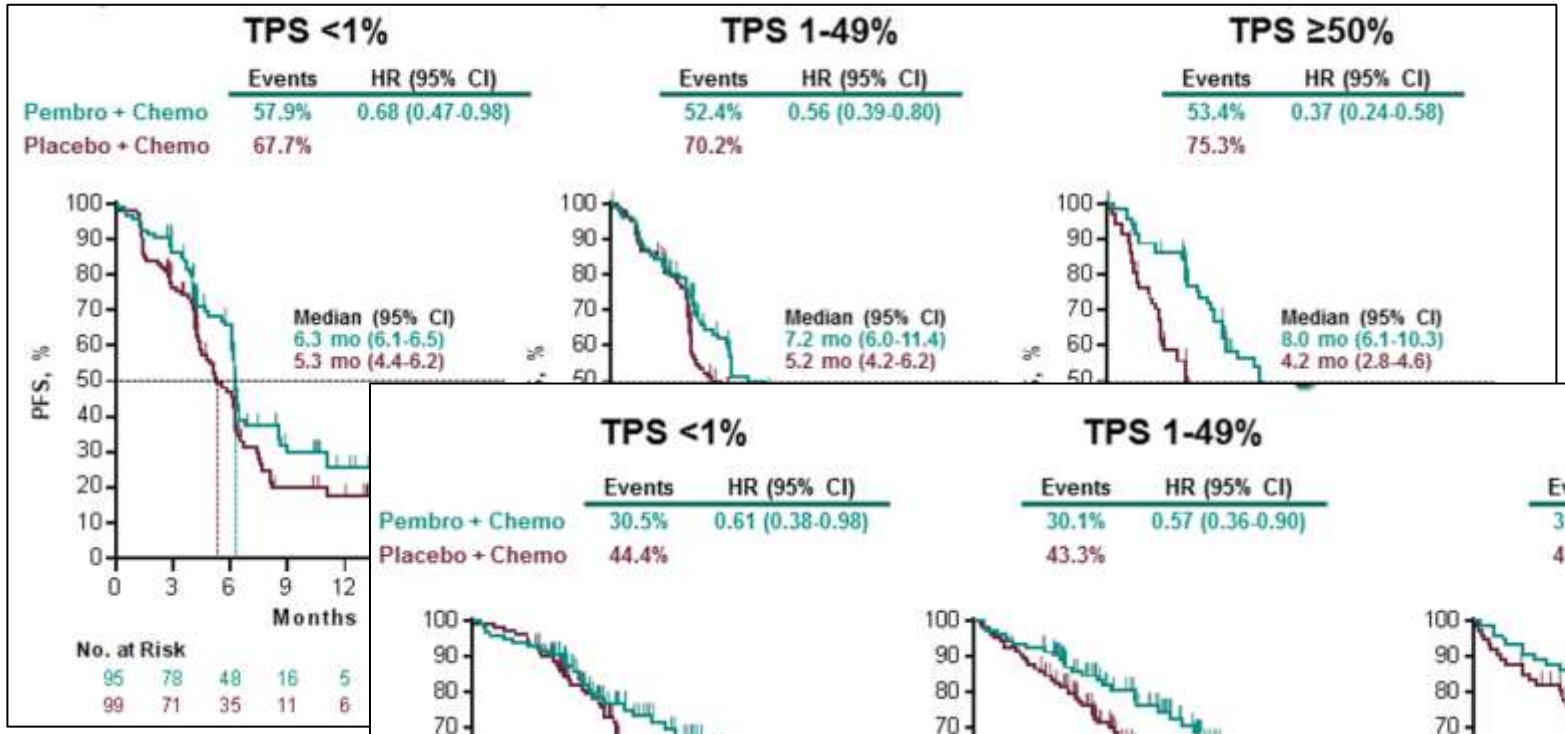


Median (95% CI)
15.9 mo (13.2-NE)
11.3 mo (9.5-14.8)

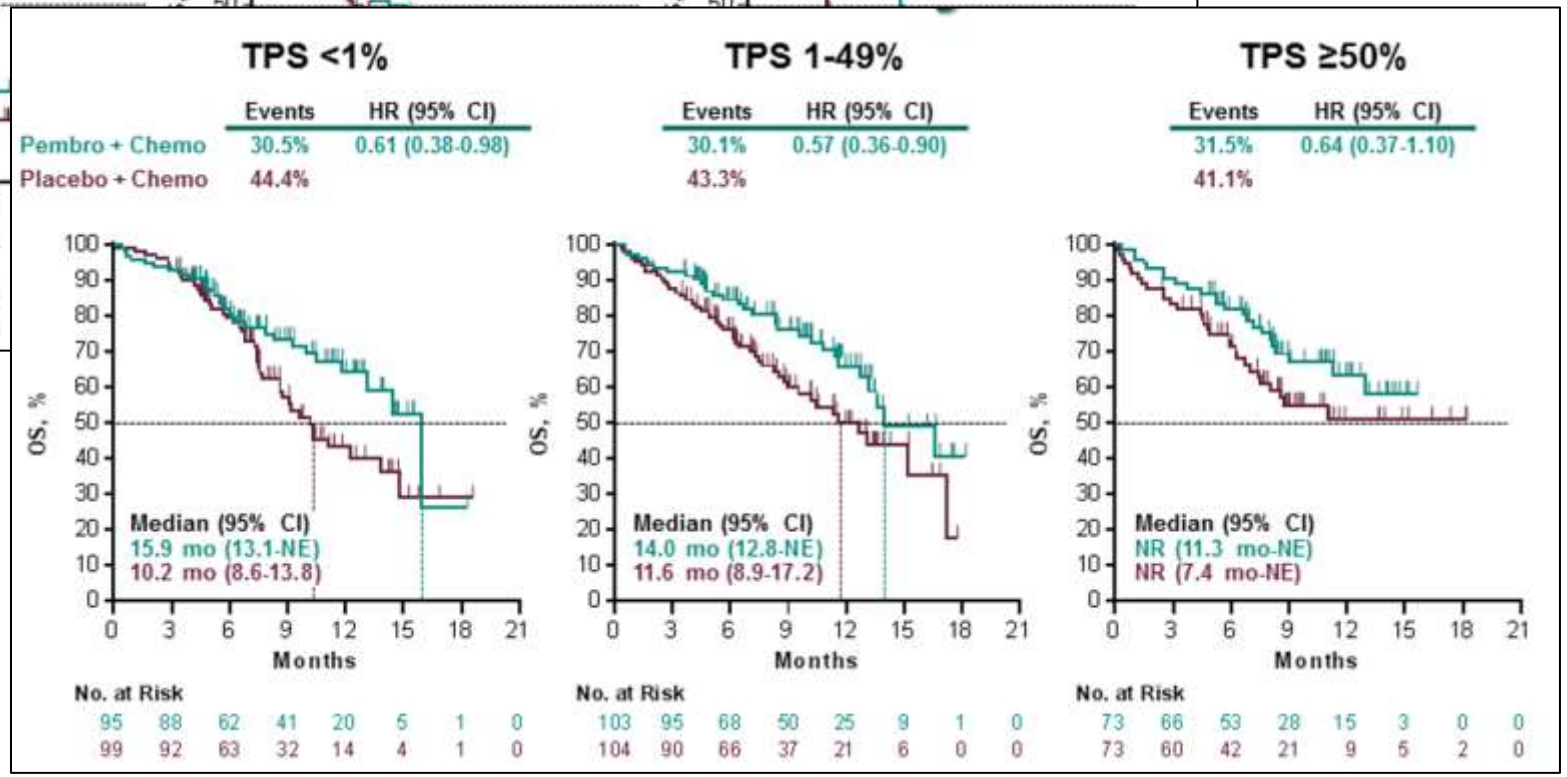
Paz-Ares L, ASCO 2018

Keynote-407: Pembrolizumab +/- chemotherapy in Sq-NSCLC

PFS

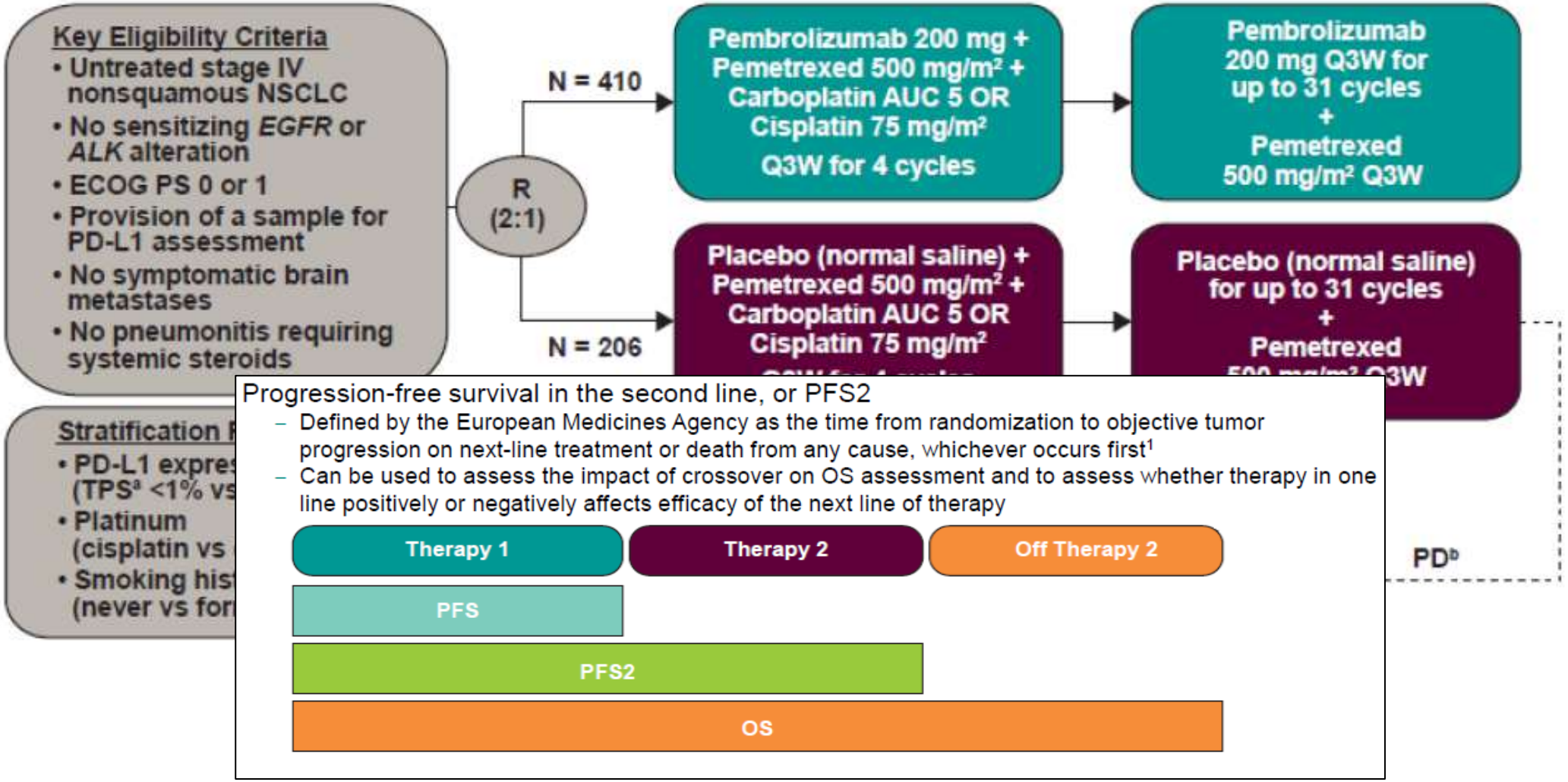


OS



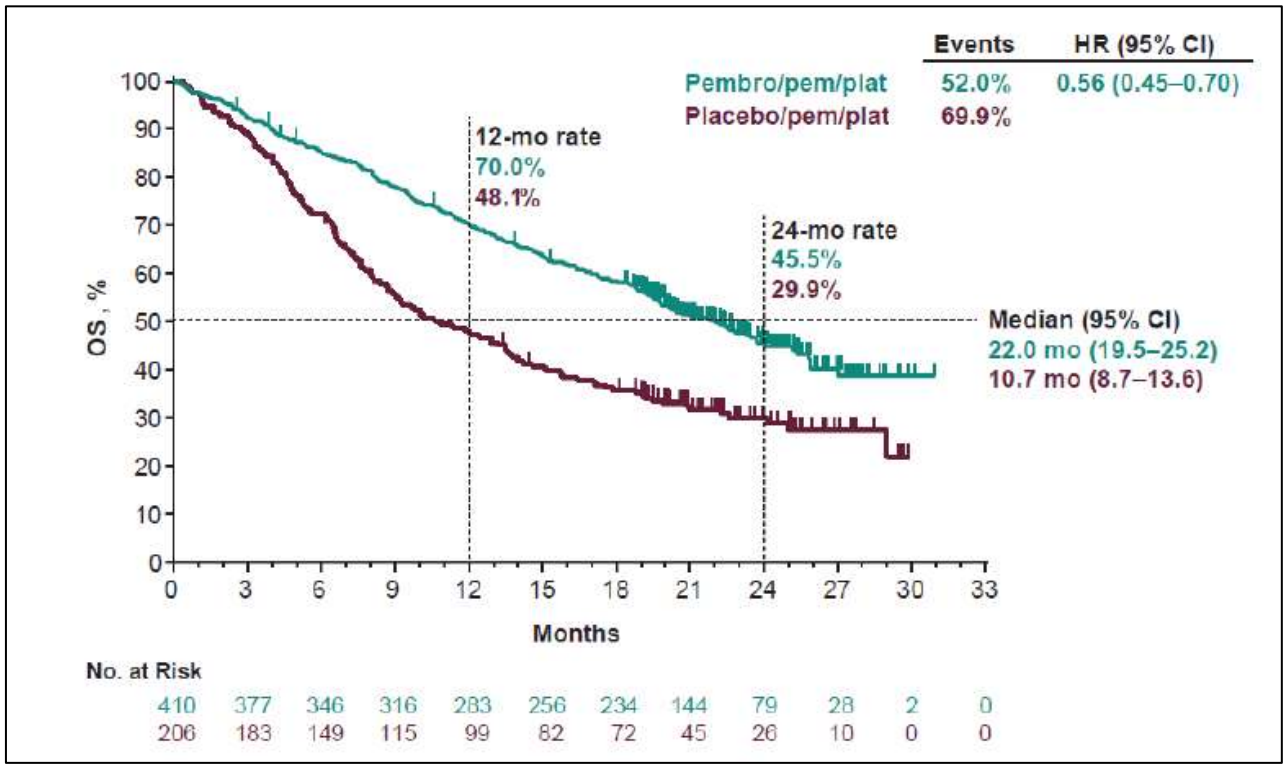
Paz-Ares L, ASCO 2018

Keynote-189: Pembrolizumab +/- chemotherapy in NONSq-NSCLC

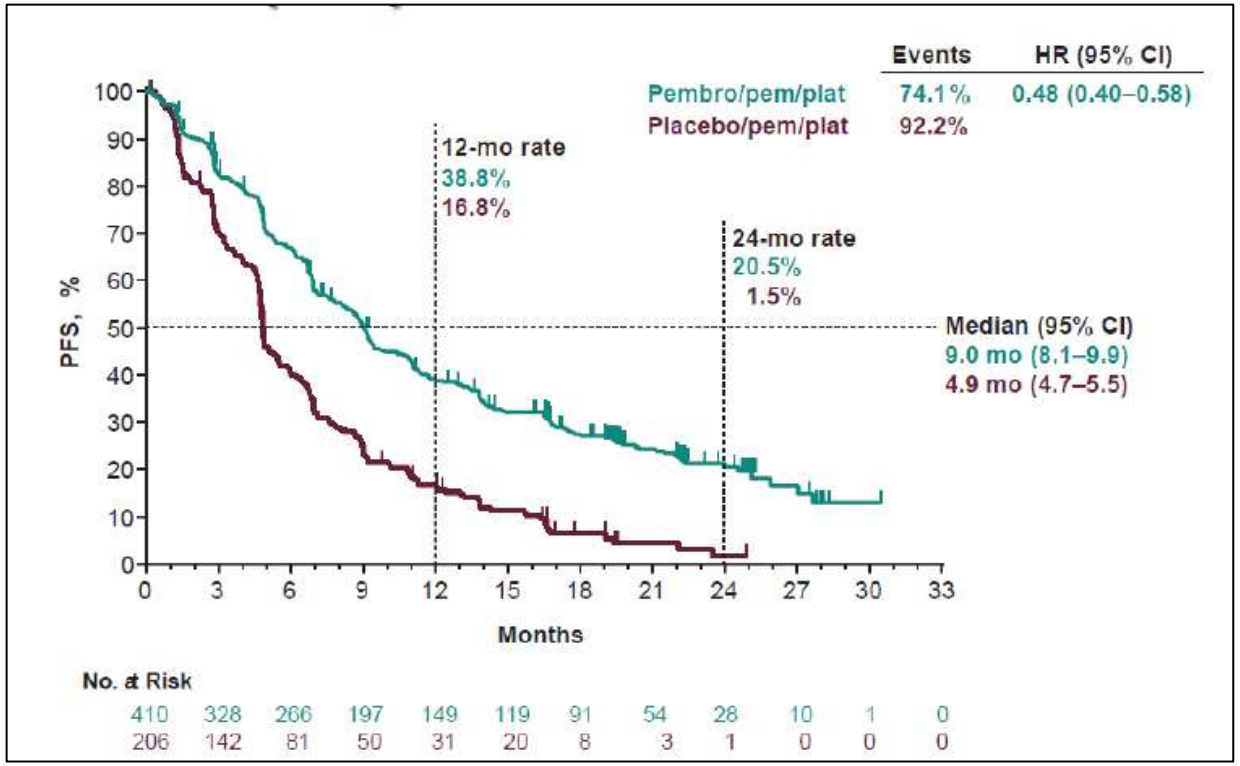


Gadgeel S, ASCO 2019

Keynote-189: Pembrolizumab +/- chemotherapy in NONSq-NSCLC



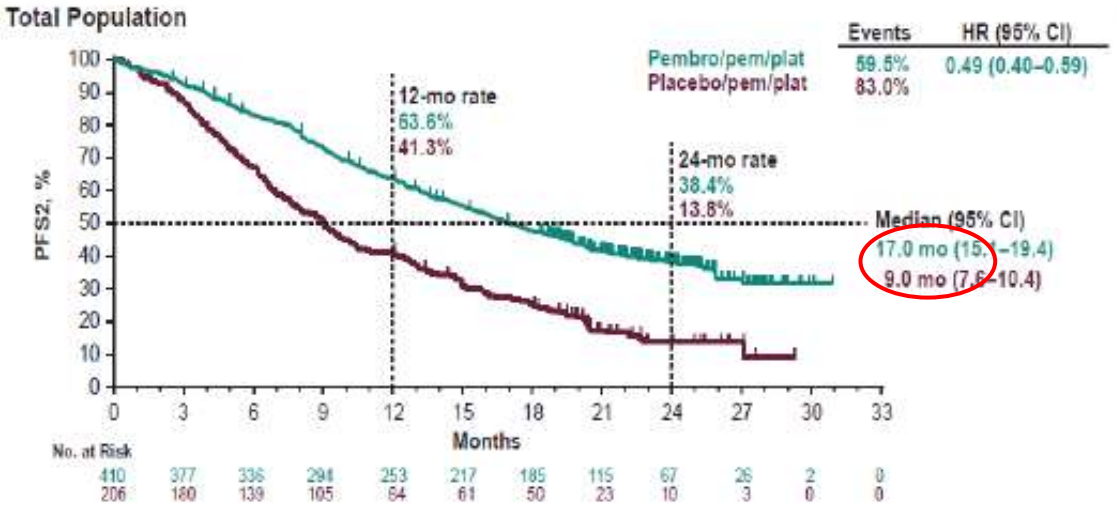
OS

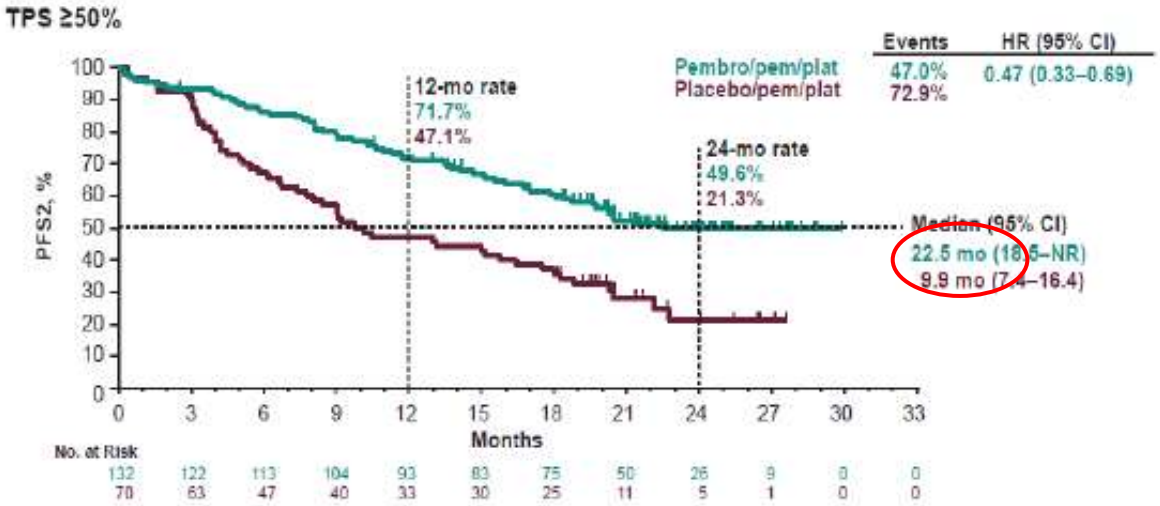


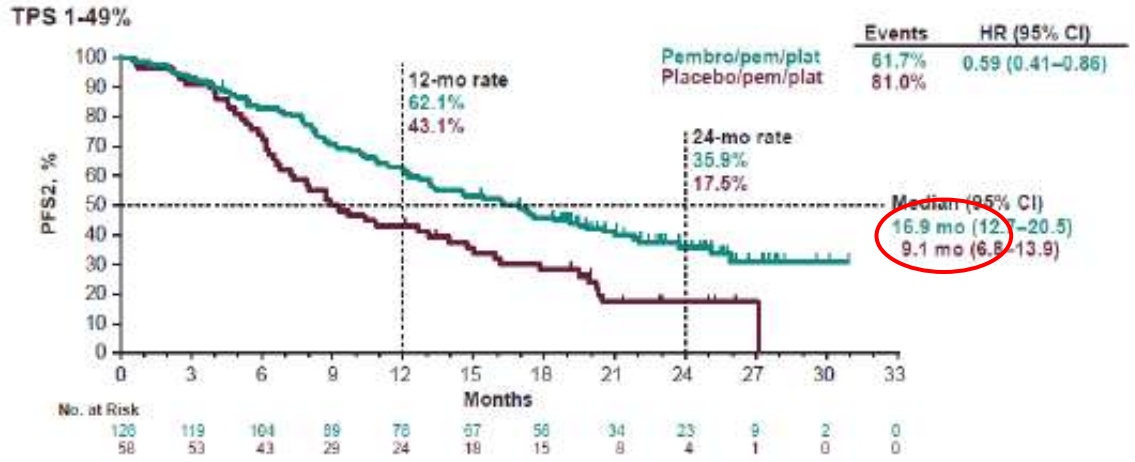
PFS

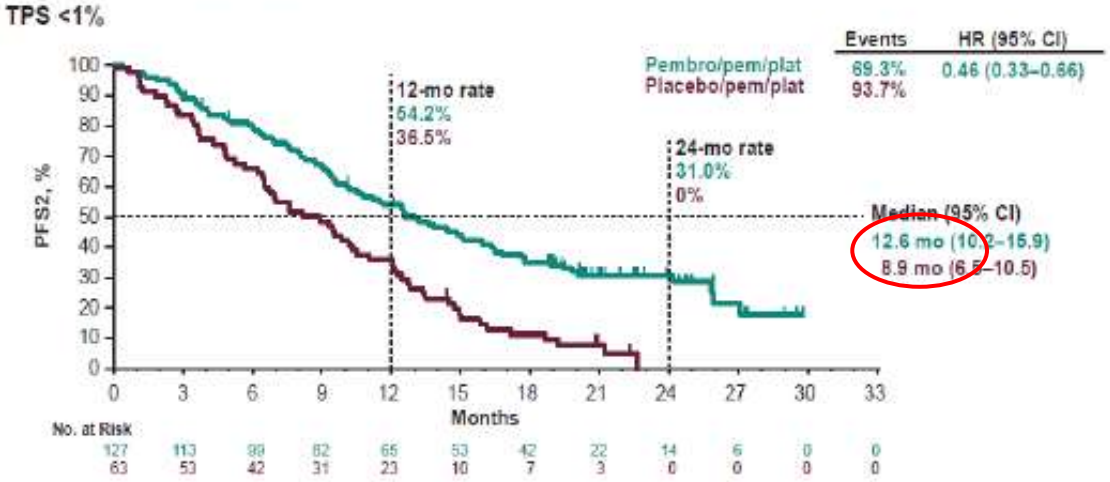
Gadgeel S, ASCO 2019

Keynote-189: PFS 2



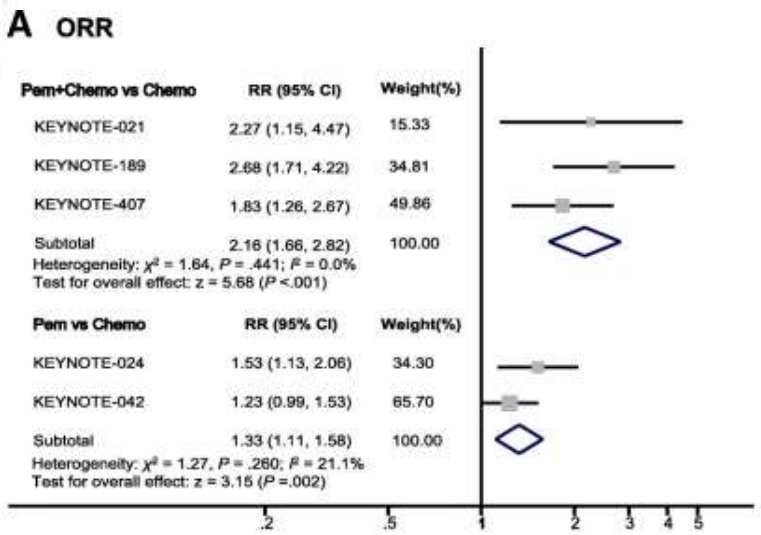


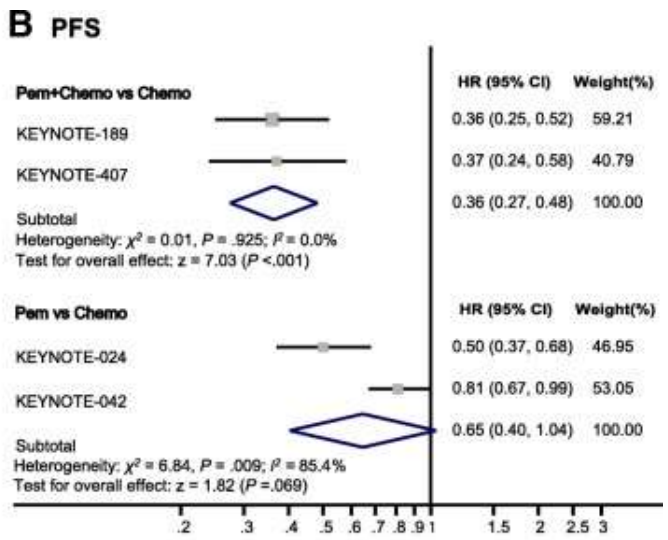


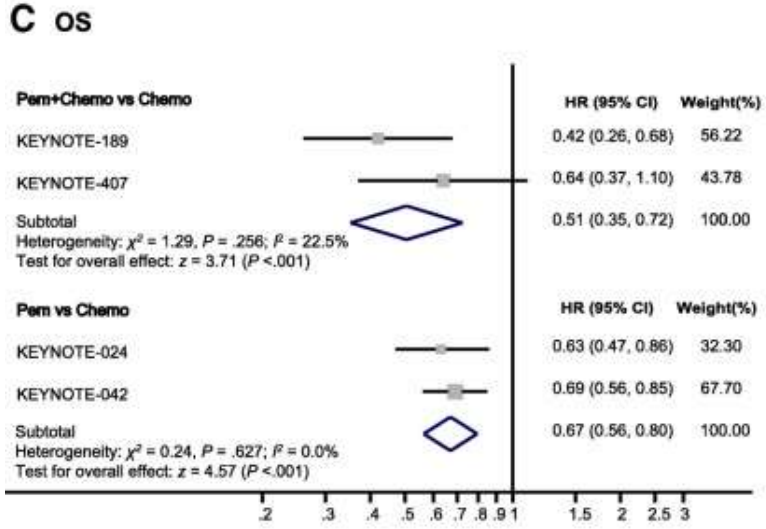


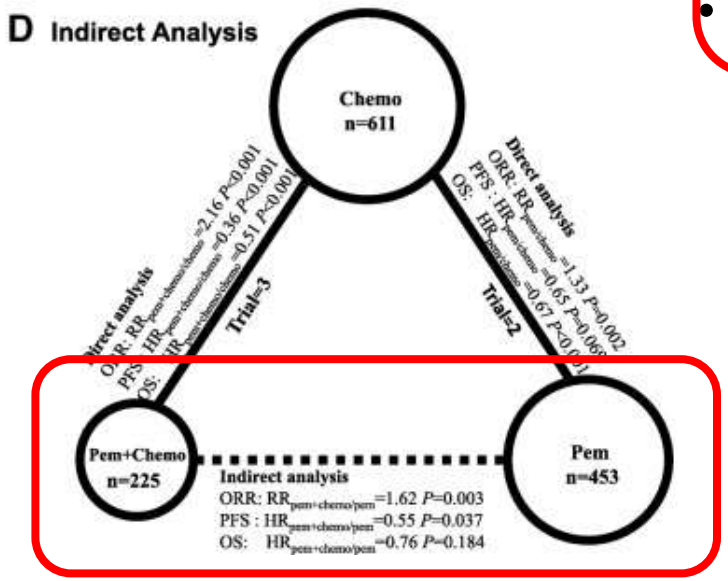
Gadgeel S, ASCO 2019

What to do in PD-L1 ≥ 50%









2-Years OS in PD-L1 ≥ 50%

- Keynote 024 (Pembro alone): 51.5%
- Keynote 189 (Pembro/CT): 51.9%

Zhou Y, et al. JITC 2019; Reck M, et al. JCO 2019, Gadjeel SM, ASCO 2019

Keynote-189: Liver and SNC mets

Baseline Characteristics

	Pembro + Pem + Platinum	Placebo
Age, median (range), years		
Men		
ECOG PS 1		
Liver metastases[a]		
Stable brain metastases[a] Previously treated		
Former/current smoker		
PD-L1 TPS ≥1%		
Carboplatin chosen		
Prior thoracic radiation		
Prior neoadjuvant therapy		
Prior adjuvant therapy		

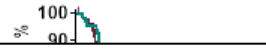
Data are shown as n (%) unless otherwise specified.
[a]25 patients had both brain and liver metastases.
Data cutoff date: September 21, 2018.

Garassino. AACR 2019

Progression-Free Survival: Liver Metastases (RECIST v1.1, BICR)

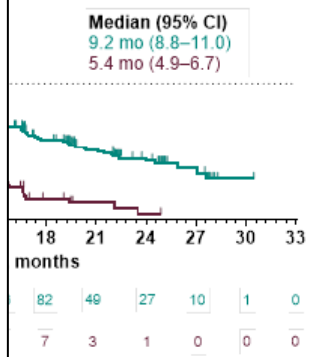
With Liver Metastases

	Events, n (%)	HR (95% CI)
Pembro/Pem/Plat	55 (83.3)	0.52 (0.34–0.81)
Placebo/Pem/Plat	47 (95.9)	



Without Liver Metastases

	Events, n (%)	HR (95% CI)
Pembro/Pem/Plat	249 (72.4)	0.48 (0.39–0.59)
Placebo/Pem/Plat	143 (91.1)	

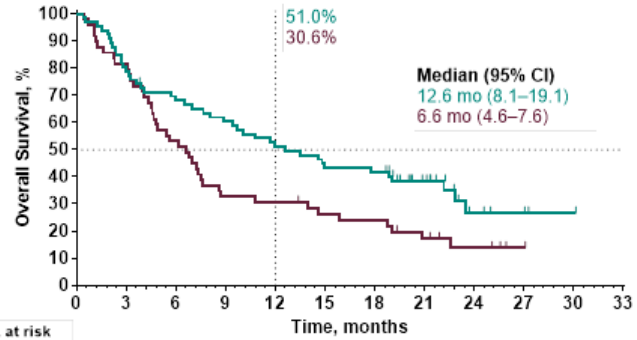


Garassino. AACR 2019

Overall Survival: Liver Metastases

With Liver Metastases

	Events, n (%)	HR (95% CI)
Pembro/Pem/Plat	43 (65.2)	0.62 (0.39–0.98)
Placebo/Pem/Plat	41 (83.7)	

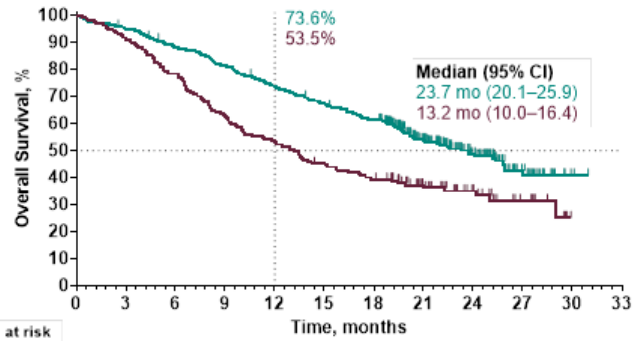


No. at risk

Pembro/Pem/Plat	66	52	45	39	33	28	27	16	5	2	1	0
Placebo/Pem/Plat	49	40	26	16	15	12	11	7	4	0	0	0

Without Liver Metastases

	Events, n (%)	HR (95% CI)
Pembro/Pem/Plat	170 (49.4)	0.58 (0.45–0.74)
Placebo/Pem/Plat	103 (65.6)	



No. at risk

Pembro/Pem/Plat	344	325	301	277	250	228	207	128	74	26	1	0
Placebo/Pem/Plat	157	143	123	99	84	70	61	38	22	10	0	0

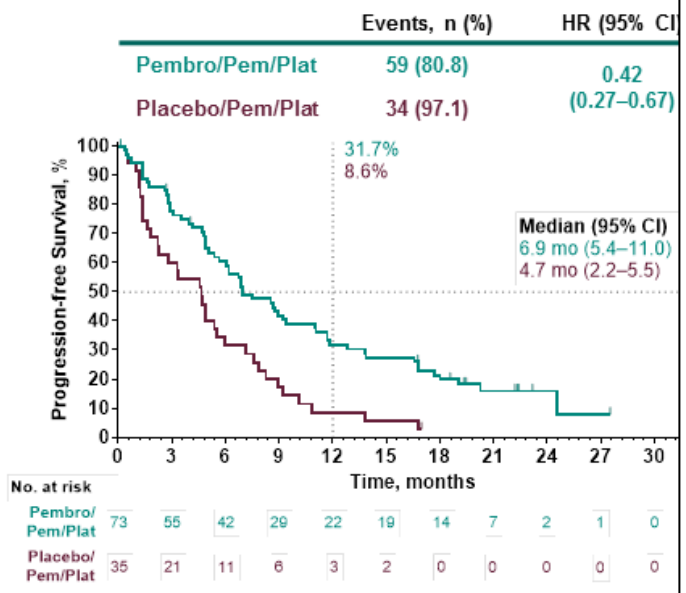
Data cutoff date: September 21, 2018.

Keynote-189: Liver and SNC mets

Garassino. AACR 2019

Progression-Free Survival: Brain Metastases (RECIST v1.1, BICR)

With Brain Metastases

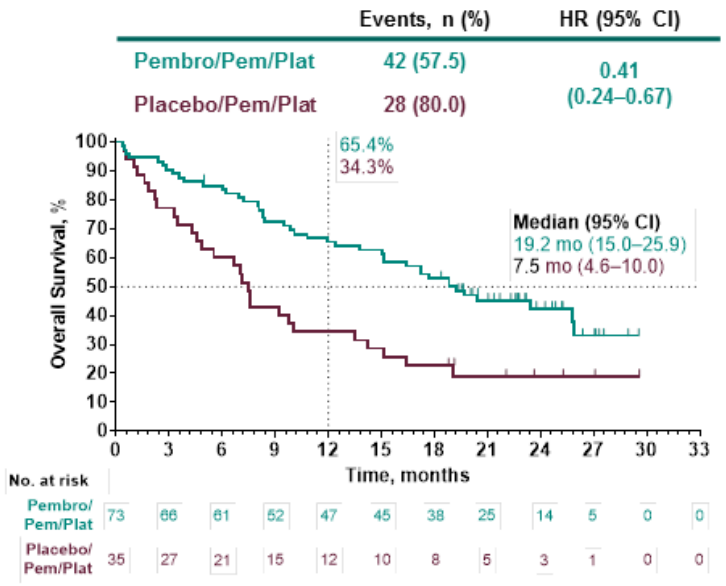


Data cutoff date: September 21, 2018.

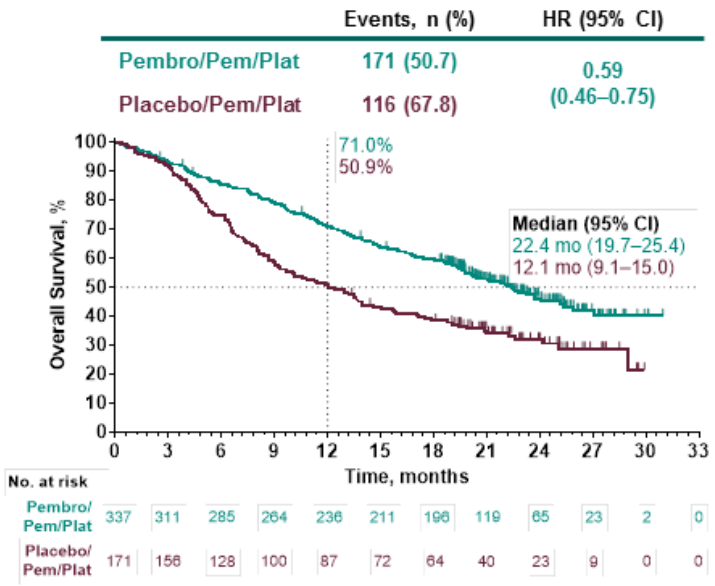
Garassino. AACR 2019

Overall Survival: Brain Metastases

With Brain Metastases

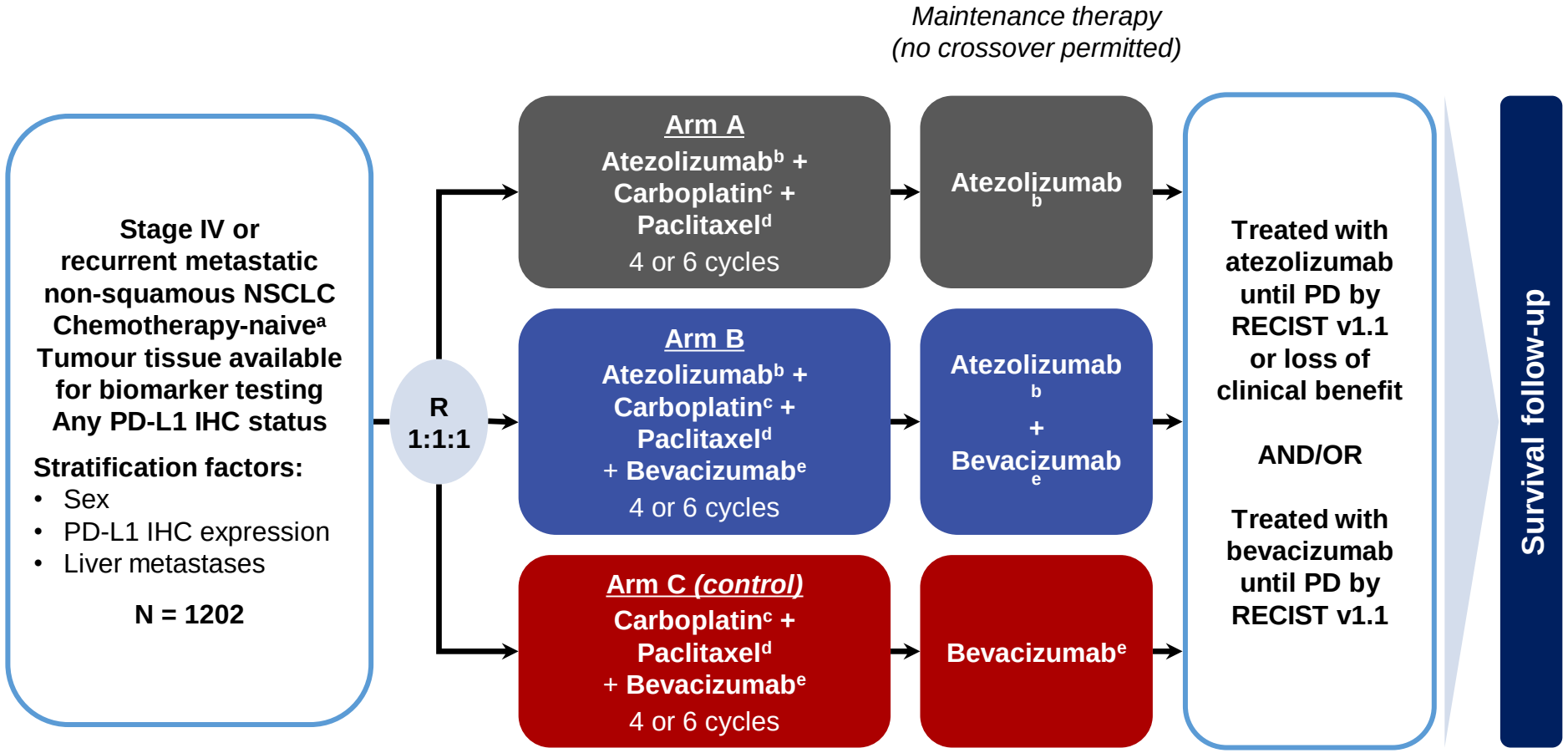


Without Brain Metastases



Data cutoff date: September 21, 2018.

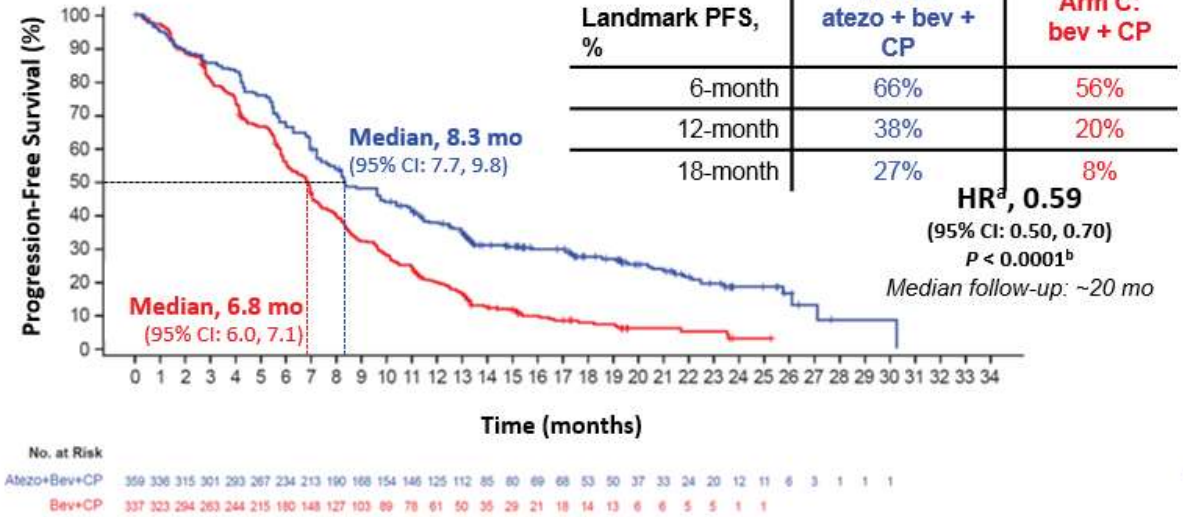
Impower-150



The principal question is to assess whether the addition of atezolizumab to Arm C provides clinical benefit

Impower-150

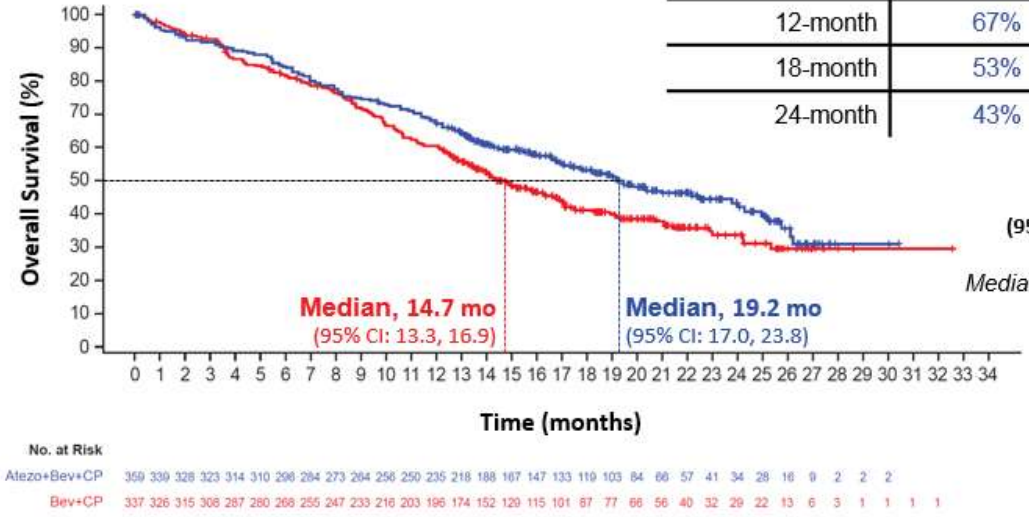
Updated PFS Analysis in the ITT-WT (Arm B vs Arm C)



Landmark PFS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
6-month	66%	56%
12-month	38%	20%
18-month	27%	8%

HR[a], 0.59
(95% CI: 0.50, 0.70)
P < 0.0001[b]
Median follow-up: ~20 mo

OS in the ITT-WT (Arm B vs Arm C)



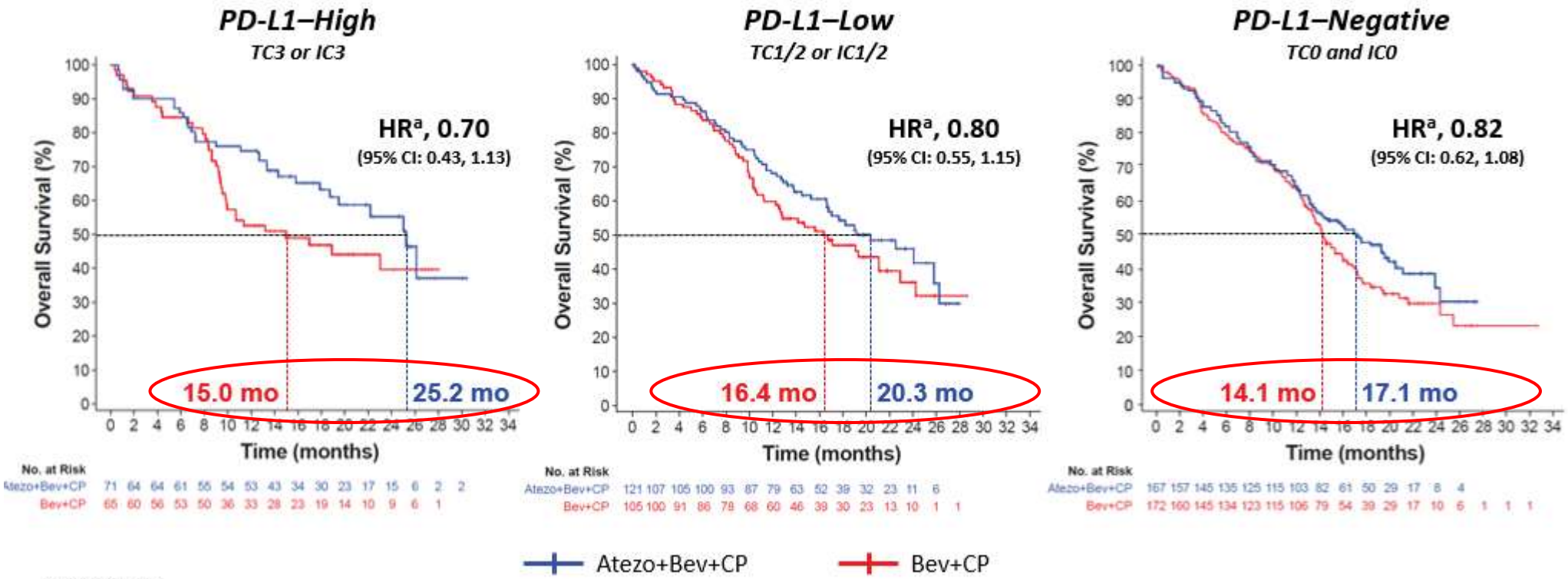
Landmark OS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
12-month	67%	61%
18-month	53%	41%
24-month	43%	34%

HR[a], 0.78
(95% CI: 0.64, 0.96)
P = 0.0164
Median follow-up: ~20 mo

Socinski MA, ASCO 2018

Impower-150

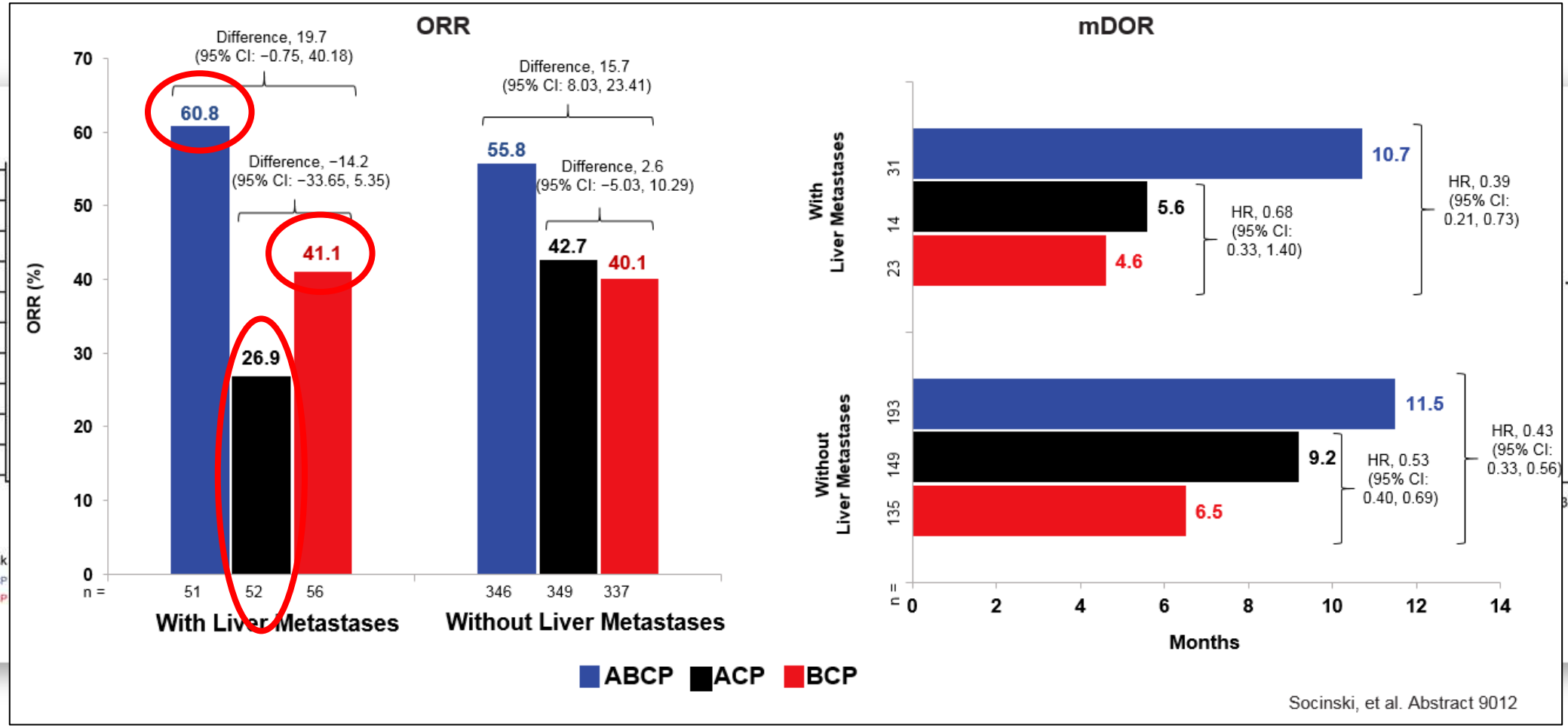
Survival Benefit Was Observed Across All PD-L1 Subgroups in the ITT-WT (Arm B vs Arm C)



[a] *Unstratified HR.*
Data cutoff: January 22, 2018

Socinski MA, ASCO 2018

Impower-150, OS according to liver mets



IrAEs in NSCLC patients: CT-IO combinations

Keynote 189 (Pembro +/- Platino-PEM)

Event, n (%)	All-Cause		Immune-Mediated and Infusion Reactions[b]	
	Pembro/Pem/ Plat n = 405	Placebo/Pem/ Plat n = 202	Pembro/Pem/ Plat n = 405	Placebo/Pem/ Plat n = 202
Any grade	404 (99.8)	200 (99.0)	107 (26.4)	
Grade 3-5	291 (71.9)	135 (66.8)	44 (10.9)	
Led to death[c]	29 (7.2)	14 (6.9)	2 (0.5)	
Led to discontinuation of any treatment component	136 (33.6)	33 (16.3)	34 (8.4)	

Impower 150 (Atezo +/- (beva)carbo-taxol)

Incidence, n (%)	Arm A: atezo + CP (n = 400)		Arm B: atezo + bev + CP (n = 393)		Arm C (*control*): bev + CP (n = 394)	
Median doses received (range), n						
Atezolizumab	10 (1-43)		12 (1-44)		NA	
Bevacizumab	NA		10 (1-44)		8 (1-38)	
Treatment-related AE[a]	377 (94%)		370 (94%)		377 (96%)	
Grade 3-4	172 (43%)		223 (57%)		191 (49%)	
Grade 5[b]	4 (1%)		11 (3%)		9 (2%)	
Serious AE	157 (39%)		174 (44%)		135 (34%)	
AE leading to withdrawal from any treatment	53 (13%)		133 (34%)		98 (25%)	
Immune-related AEs[c] in > 5 patients in any arm	**All grade**	**Grade 3-4**	**All grade**	**Grade 3-4**	**All grade**	**Grade 3-4**
Rash	119 (30%)	14 (4%)	117 (30%)	9 (2%)	53 (14%)	2 (1%)
Hepatitis[d]	42 (11%)	12 (3%)	54 (14%)	20 (5%)	29 (7%)	3 (1%)
Laboratory abnormalities	36 (9%)	10 (3%)	48 (12%)	18 (5%)	29 (7%)	3 (1%)
Hypothyroidism	34 (9%)	1 (<1%)	56 (14%)	1 (<1%)	18 (5%)	0
Pneumonitis[d]	23 (6%)	8 (2%)	13 (3%)	6 (2%)	5 (1%)	2 (1%)
Hyperthyroidism	11 (3%)	0	16 (4%)	1 (<1%)	5 (1%)	0
Colitis	3 (1%)	2 (1%)	11 (3%)	7 (2%)	2 (1%)	2 (1%)

The safety profiles of ABCP and ACP were similar to A, B and C+P individually; no new safety signals were identified with the combinations

All cause AEs		
Grade 3-5		
Led to death		
Treatment-related		
Led to discontinuation		
All treatment[a]	37 (13.3%)	18 (6.4%)
Any treatment	65 (23.4%)	33 (11.8%)
Immune mediated AEs and infusion reactions	80 (28.8%)	24 (8.6%)
Grade 3-5	30 (10.8%)	9 (3.2%)
Led to death[b]	1 (0.4%)	1 (0.4%)

Keynote 407 (Pembro +/- Platino-(nab)paclitaxel)

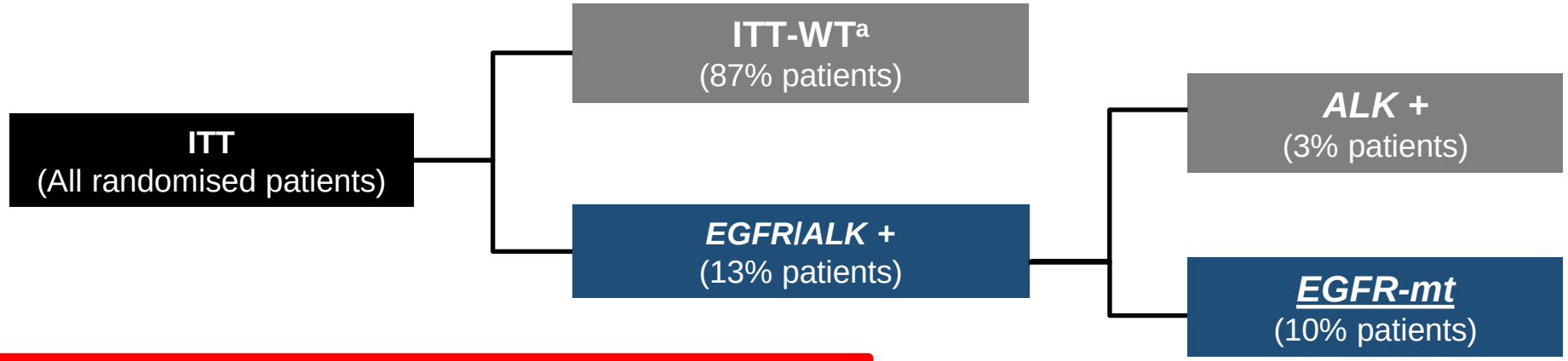
Socinsli MA, ASCO 2018; Paz-Ares L, ASCO 2018; Gadgeel ASCO 2019

Agenda

- NSCLC stage IV, first line (wild type)
- **NSCLC stage IV, oncogene addicted**
- What we've learned from IO-clinical practice
- Conclusions

Impower-150, oncogene addicted population

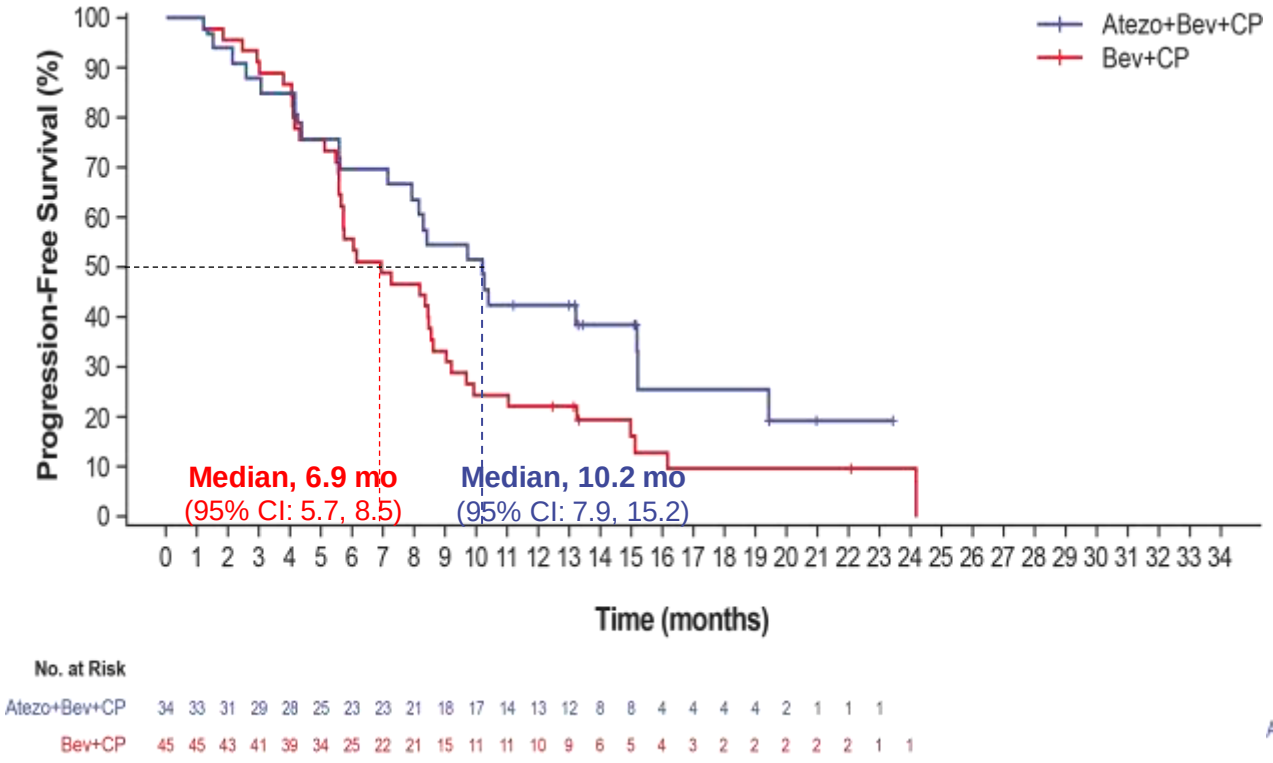
- The efficacy and safety of atezolizumab and/or bevacizumab with chemotherapy is being further analysed in the subpopulation of patients with EGFR mutations



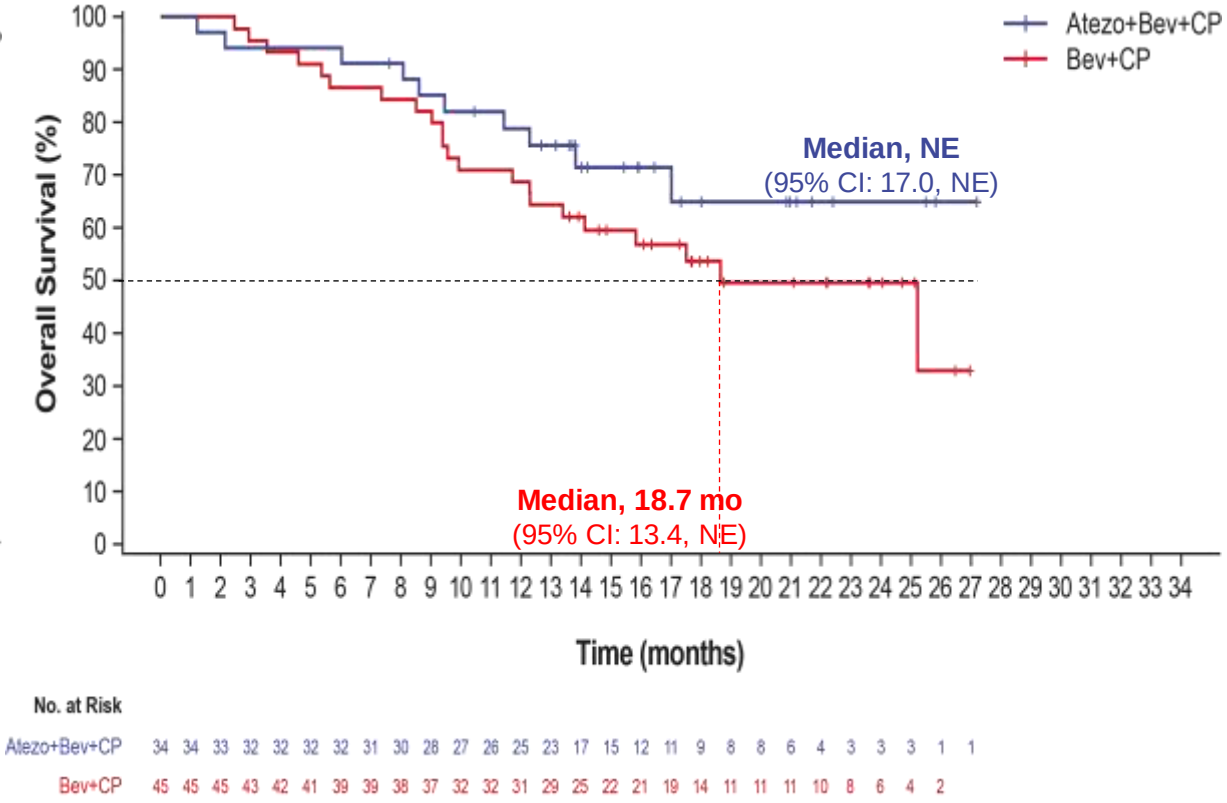
[a] **Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.**

Reck M, elcc 2019

Impower-150, *EGFR* positive population



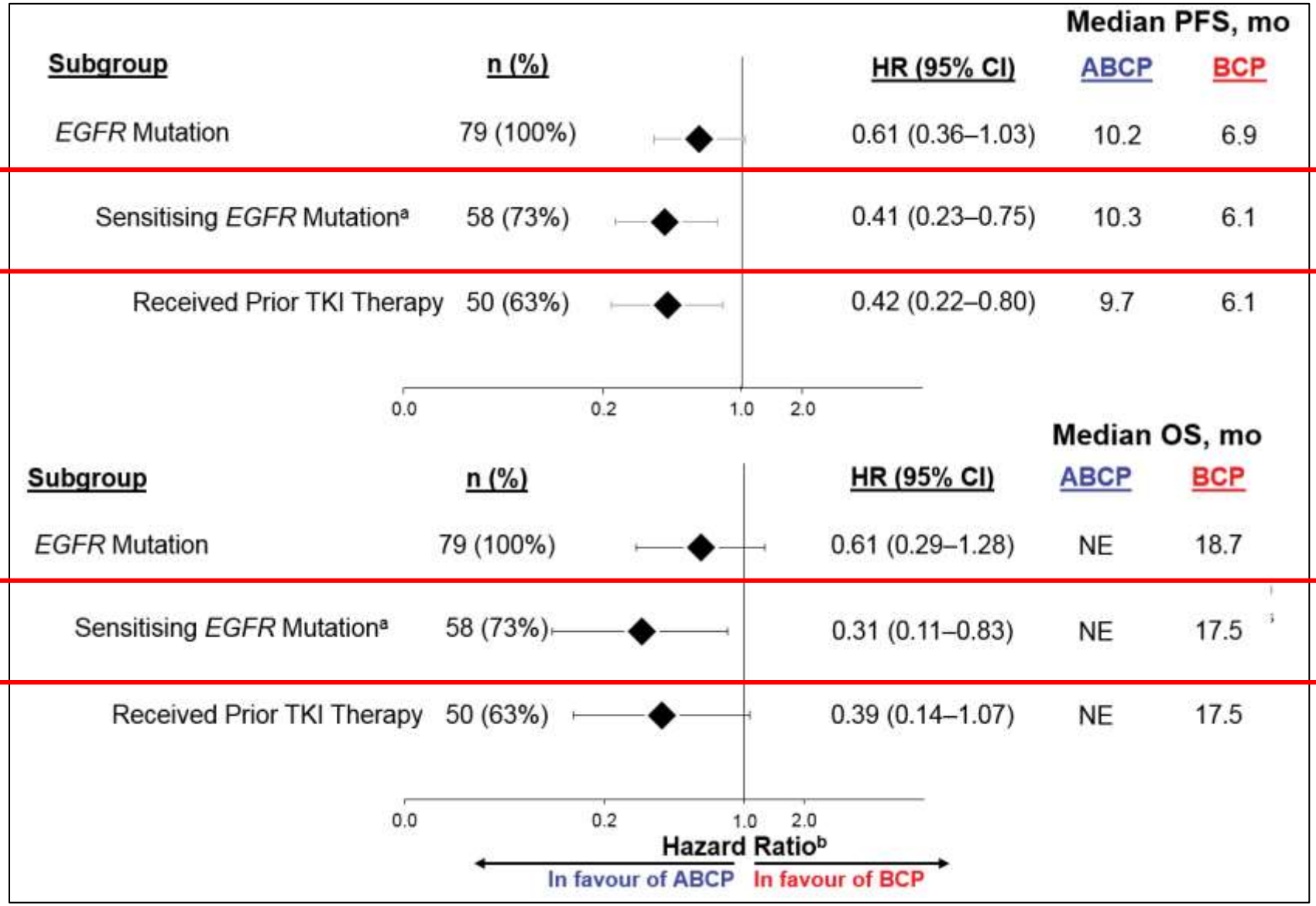
Progression Free Survival



Overall Survival

Reck M, elcc 2019

Impower-150, *EGFR* positive population



Reck M, elcc 2019

Impower-130, *EGFR* positive population

IMpower130 study design

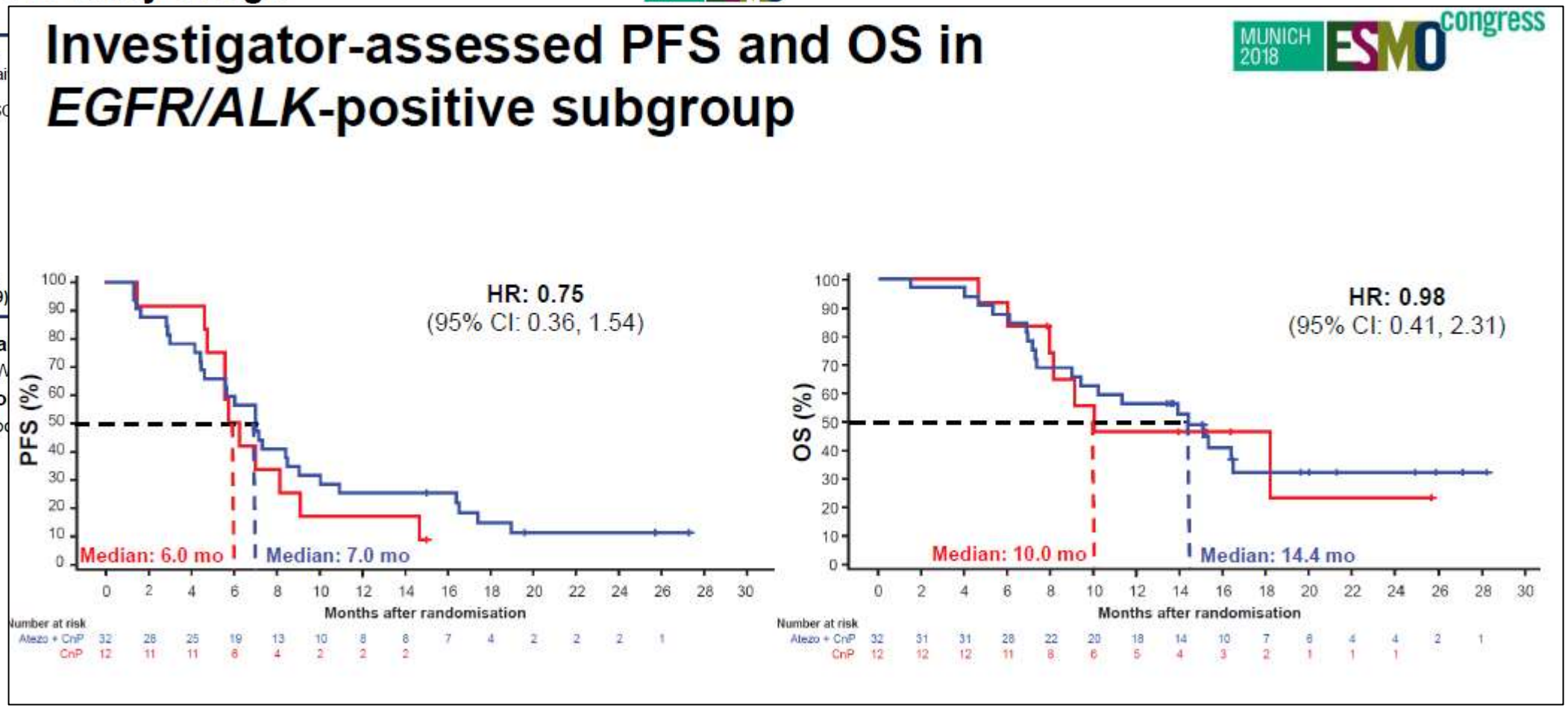
Patients with chemotherapy-nai
stage IV
non-squamous NSC

Stratification:
- Sex
- Baseline liver metastases
- PD-L1 tumour expression

(ITT: N=723;
ITT-WT: n=679)

- **Co-prima**
  - ITT-W
- **Key seco**
  - ITT p

Investigator-assessed PFS and OS in *EGFR/ALK*-positive subgroup



Cappuzzo F, ESMO 2018

Agenda

- NSCLC stage IV, first line (wild type)
- NSCLC stage IV, oncogene addicted
- **What we've learned from IO-clinical practice**
- Conclusions

Liver mets, second line setting

Botticelli et al. J Transl Med (2019) 17:99
https://doi.org/10.1186/s12967-019-1847-x

Journal of Translational Medicine

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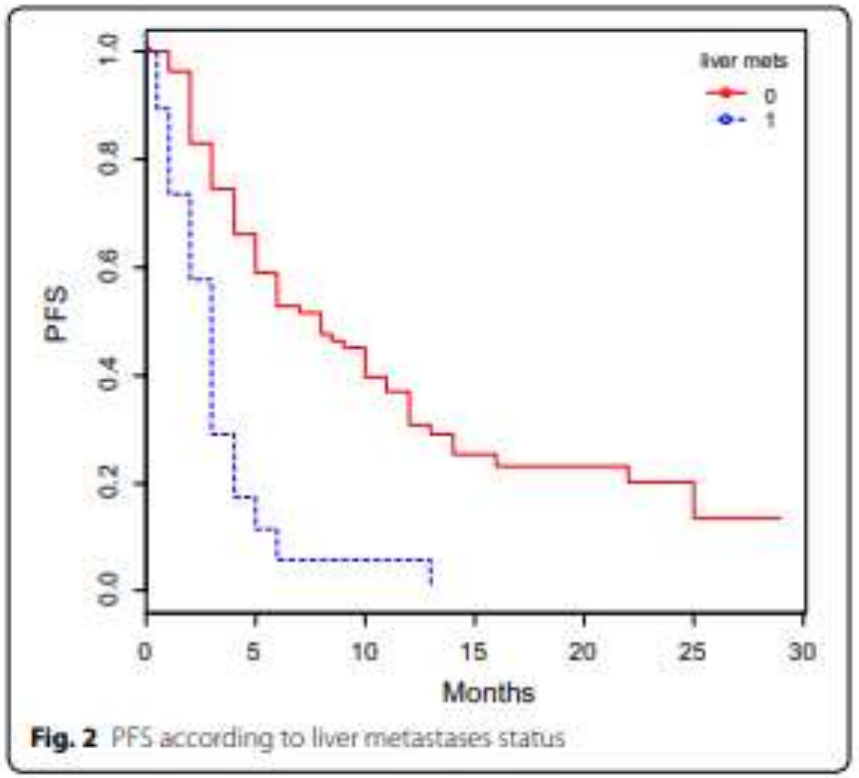


Fig. 2 PFS according to liver metastases status

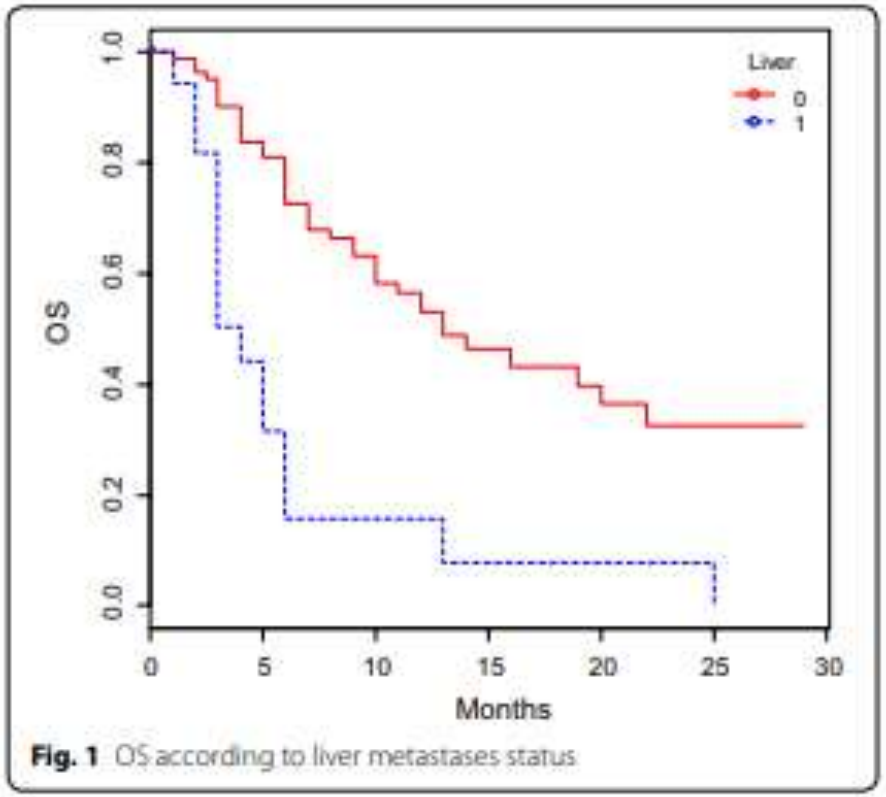
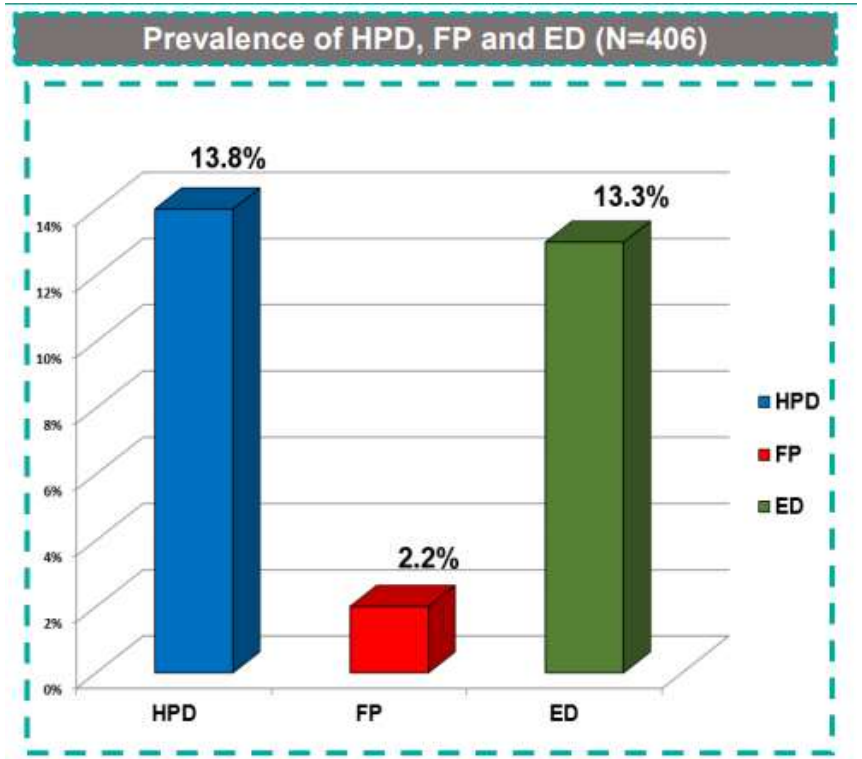


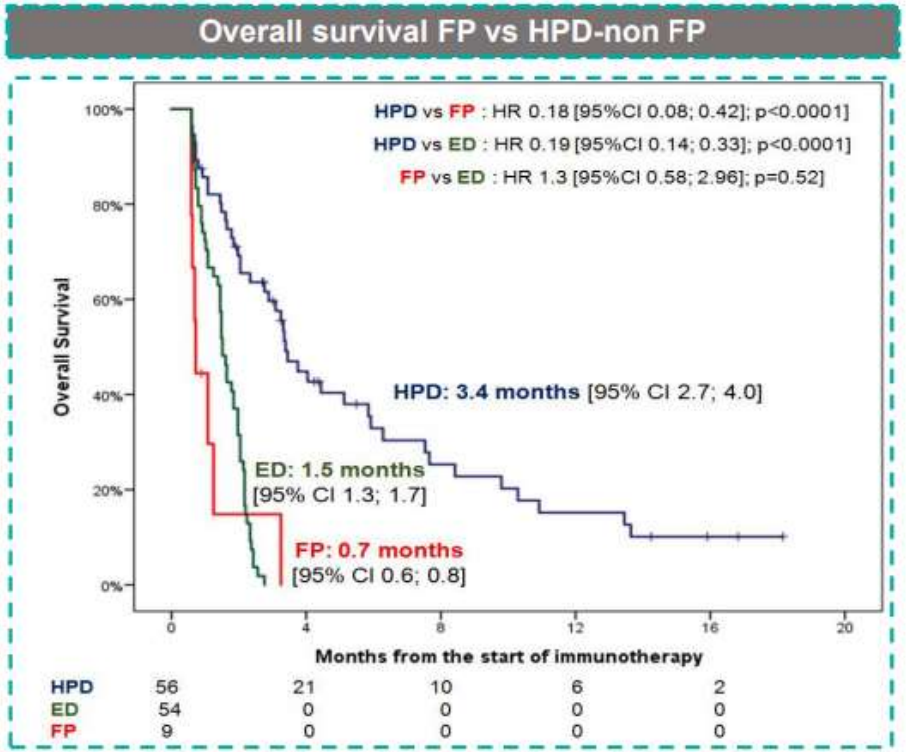
Fig. 1 OS according to liver metastases status

Botticelli A, et al. JTM 2019

Fast Progressors: an unmet medical need

- 5 out of 20 NSCLC patients treated with 1stline pembrolizumab were retrospectively collected had **HPD** (defined by Time to Treatment Failure ≤2 months and raising in Tumor Burden ≥50% compared with basal CT-scan)
- **HPD** was defined as RECIST v 1.1 PD at first CT scan and a >50% TGR variation per month, **FP** was defined as ≥ 50% increase in the sum of long diameters within 6 weeks from baseline, **ED** was defined as deaths due to disease PD within 12 weeks of IO start





Giusti R, et al. ASCO 2019; Ferrara R, et al. ASCO 2019

Baseline corticosteroids: needing for clarification

- **93 (14.3%) out of 650 patients received ≥ 10 mg of prednisone at the time of immunotherapy**
- **When analyzed by reason for corticosteroid administration, mPFS and mOS were significantly shorter only among patients who received ≥ 10 mg prednisone for palliative indications**
- **There was no significant difference in mPFS or mOS in patients receiving ≥ 10 mg of prednisone for cancer-unrelated indications compared with patients receiving 0 to < 10 mg of prednisone.**

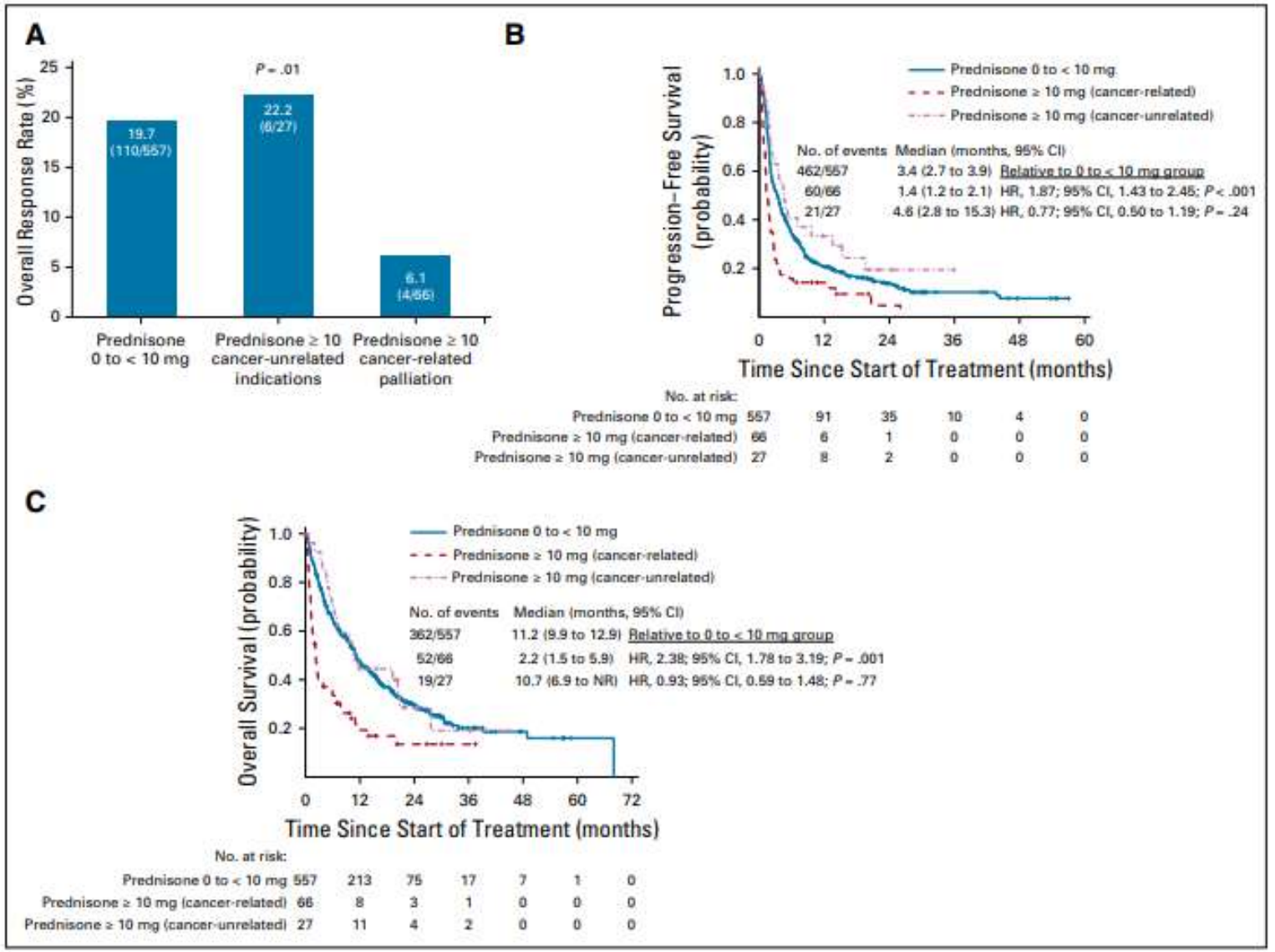


FIG 3. Outcomes to immunotherapy in the group of patients treated with ≥ 10 mg of prednisone for cancer-related palliative indications or cancer-unrelated indications compared with the group of patients receiving less than 10 mg of prednisone according to (A) overall response rate, (B) progression-free survival (PFS), and (C) overall survival (OS). HR, hazard ratio; NR, not reached.

Ricciuti B, et al. JCO 2019

2019 NEWS IN ONCOLOGY

Patients with Autoimmune Diseases

The Oncologist®

Immuno-Oncology

Clinical Outcomes of Patients with Advanced Cancer and Pre-Existing Autoimmune Diseases Treated with Anti-Programmed Death-1 Immunotherapy: A Real-World Transverse Study

Alessio Cortellini,[a,b] Sebastiano Buti,[c] Daniele Santini,[d] Fabiana Perrone,[c] Raffaele Giusti,[e] Marcello Tiseo,[c] Melissa Bersanelli,[c] Maria Michiara,[c] Antonino Grassadonia,[f] Davide Brocco,[g] Nicola Tinari,[f] Michele De Tursi,[f] Federica Zoratto,[h] Enzo Veltri,[h] Riccardo Marconcini,[i] Francesco Malorgio,[j] Carlo Garufi,[j] Marco Russano,[d] Cecilia Anesi,[d] Tea Zeppola,[d] Marco Filetti,[e] Paolo Marchetti,[a,k] Andrea Botticelli,[a] Gian Carlo Antonini Cappellini,[k] Federica De Galitiis,[k] Maria Giuseppa Vitale,[l] Roberto Sabbatini,[l] Sergio Bracarda,[m] Rossana Berardi,[n] Silvia Rinaldi,[n] Marianna Tudini,[o] Rosa Rita Silva,[o] Annagrazia Pireddu,[p] Francesco Atzori,[p] Rita Chiari,[q] Biagio Ricciuti,[q] Daniela Iacono,[r] Maria Rita Migliorino,[r] Antonio Rossi,[s] Giampiero Porzio,[a,b] Katia Cannita,[b] Valeria Ciciarelli,[t,b] Maria Concetta Fargnoli,[t,b] Paolo Antonio Ascierto,[u] Corrado Ficorella[a,b]

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Anti-programmed death-1 • Sex • Autoimmune disease • Immunotherapy • Performance status • Immune checkpoint inhibitors

Table 2. List of pre-existing autoimmune disease and immunosuppressant treatments

AIDs and treatments	*n* (%)	Specifications
Pre-existing AIDs	85	
Thyroid disorders	51 (60)	10 GBD, 51 hypothyroidism after AIT
Dermatologic	14 (16.4)	11 PSO, 2 vitiligo, 1 lichen planus
Rheumatologic	10 (11.8)	2 PMR, 2 SLE, 4 AR, 1 vasculitis
Gastrointestinal/hepatic	4 (4.7)	3 CD, 1 PSC
Neurologic	1 (1.2)	1 AI optic neuritis
Nephrologic	1 (1.2)	1 membranous glomerulonephritis
Multiple site	4 (4.7)	1 GBS and PSO, 1 MG and AIT, 1 PSO and AIT, 1 scleroderma and AIT
Clinically active AIDs	15	
Dermatologic	6 (40)	6 PSO
Rheumatologic	6 (40)	4 RA, 2 PMR
Gastrointestinal	2 (13.3)	2 CD
Multiple site	1 (6.6)	1 scleroderma and AIT
Treatment of AIDs		
Corticosteroids	11 (73.3)	4 PSO, 1 scleroderma and AIT, 3 RA, 2 PMR, 1CD
Other immunosuppressants	3 (20)	1 RA, 2 PSO
Combinations	1 (6.6)	1 CD

Abbreviations: AIDs, autoimmune diseases; AIT, autoimmune thyroiditis; CD, Crohn's disease; GBD, Graves-Basedow disease; GBS, Guillain-Barre syndrome; MG, myasthenia gravis; PMR, polymyalgia rheumatica; PSC, primary sclerosing cholangitis; PSO, psoriasis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Cortellini A, et al. Oncologist 2019

Patients with Autoimmune Diseases

irAEs of any grade—multivariate analysis			
Variable (comparator)	**Coefficient**	**Standard error**	***p* value**
Pre-existing AIDs (No AIDs)			
Inactive	0.9314	0.2673	.0005
Active	1.4452	0.6011	.0162
Primary tumor			
(NSCLC)	—	—	
Melanoma	0.2726	0.1891	.1496
Kidney	0.4046	0.2326	.0820
Others	—	—	.9977
Sex	−0.5762	0.1613	.0004
ECOG-PS	−0.7432	0.2504	.0030
Nagelkerke R^2 0.0961			

[a]Binomial confidence interval.
Abbreviations: —, no data; AIDs, autoimmune diseases; CI, confidence interval; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; irAEs, immune-related adverse events; NSCLC, non-small cell lung cancer.

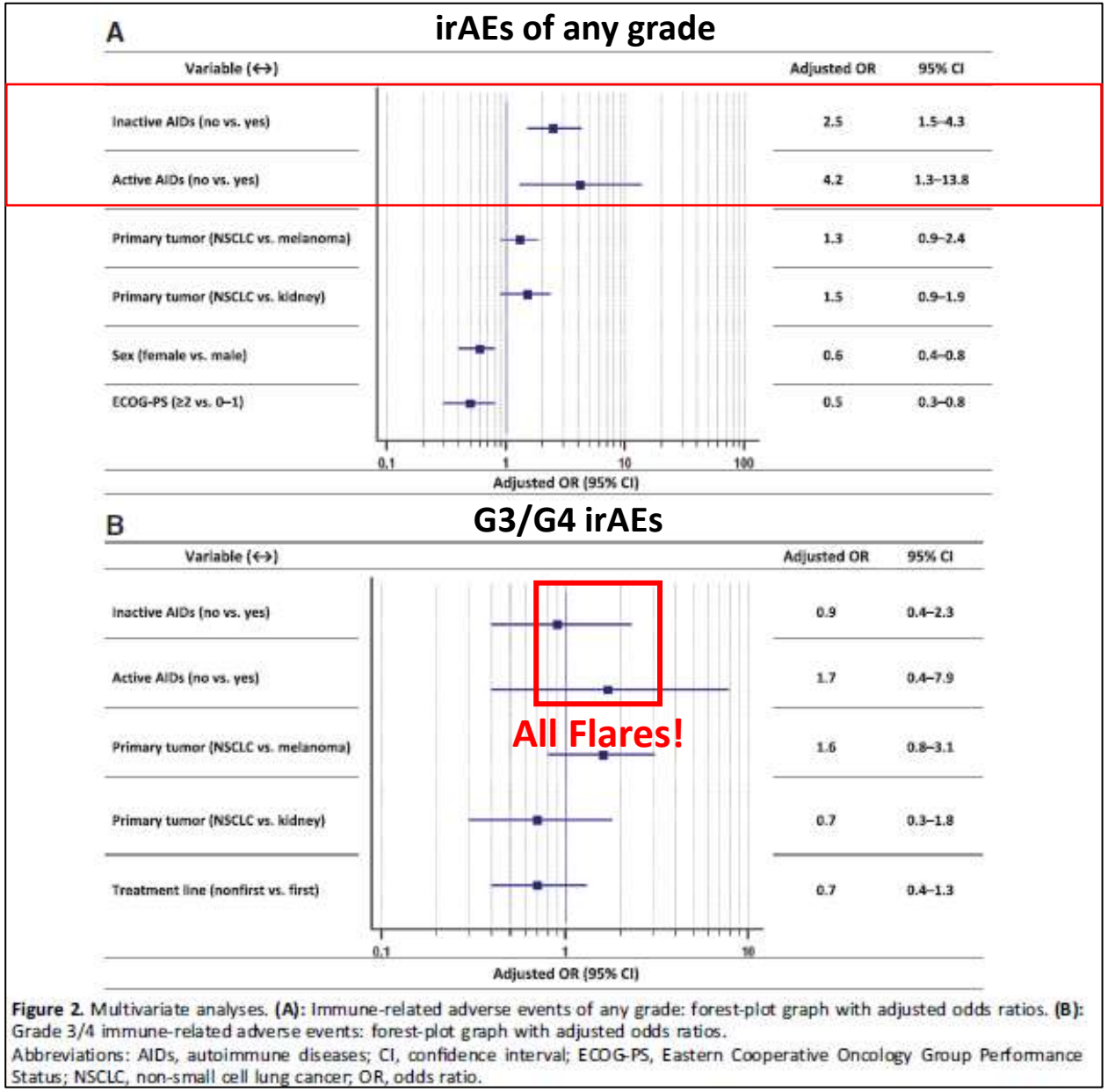

Figure 2. Multivariate analyses. **(A):** Immune-related adverse events of any grade: forest-plot graph with adjusted odds ratios. **(B):** Grade 3/4 immune-related adverse events: forest-plot graph with adjusted odds ratios.
Abbreviations: AIDs, autoimmune diseases; CI, confidence interval; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; NSCLC, non-small cell lung cancer; OR, odds ratio.

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IrAEs in NSCLC patients: real-life

	559
AGE, (years)	
Median	69
Elderly (≥ 70)	259 (46.3)
SEX	
Male	379 (67.8)
ECOG PS	
≥ 2	74 (13.3)
Histology	
Squamous	235 (42.1)
No. of metastatic sites	
> 2	317 (56.8)
Type of anti-PD-1	
Pembrolizumab	123 (22)
Nivolumab	436 (78)
Line of Immunotherapy	
First	116 (20.8)
irAEs	**231 (41.3)**
Single Site	191 (82.6)
Multiple Site	40 (17.4)
PD-L1 expression (TPS)	
Not-available	354 (63.3)
Negative	45 (8.1)
1 – 49%	60 (10.7)
≥ 50%	100 (17.9)

	irAEs of any grade	G3/G4 irAEs
Patients	**231**	**50**
Endocrine	78 (33.8)	4 (8)
Gastrointestinal	51 (22.1)	15 (30)
Skin	59 (24.2)	7 (14)
Pneumological	23 (9.9)	12 (24)
Haepatic	10 (4.3)	6 (12)
Others	46 (19.9)	6 (12)

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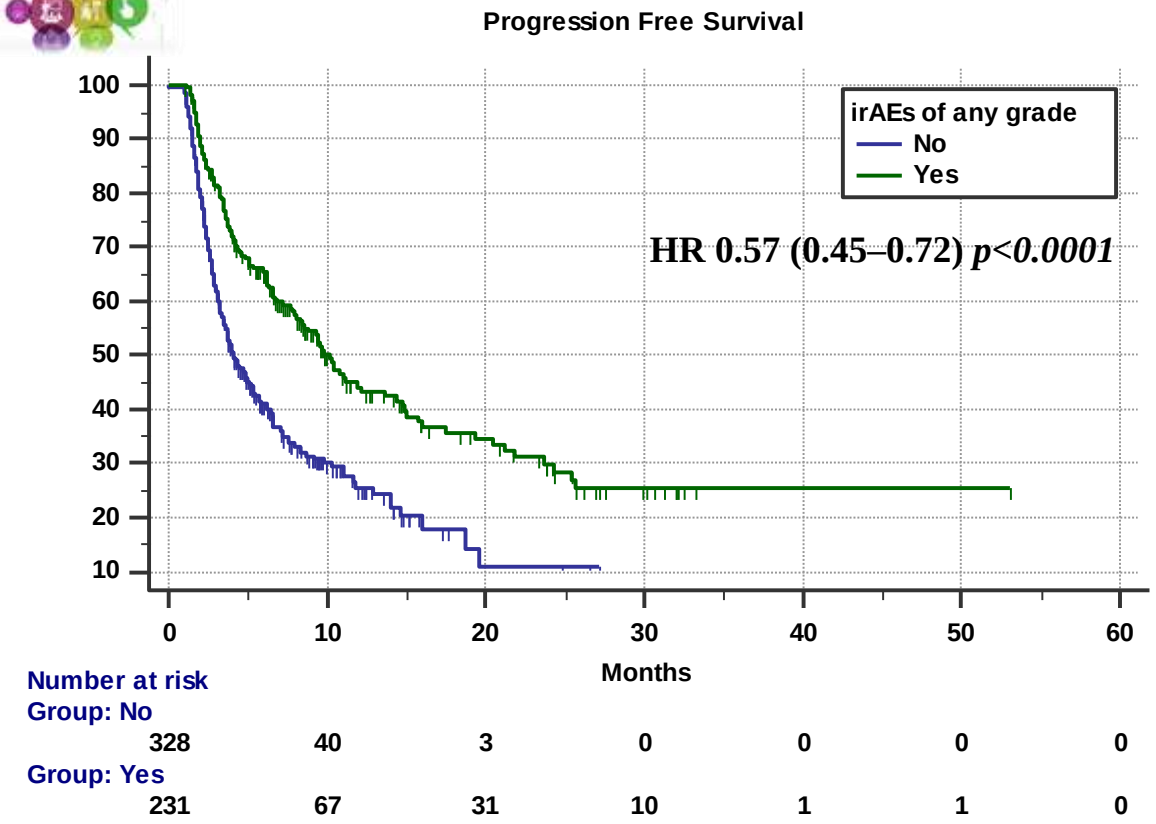
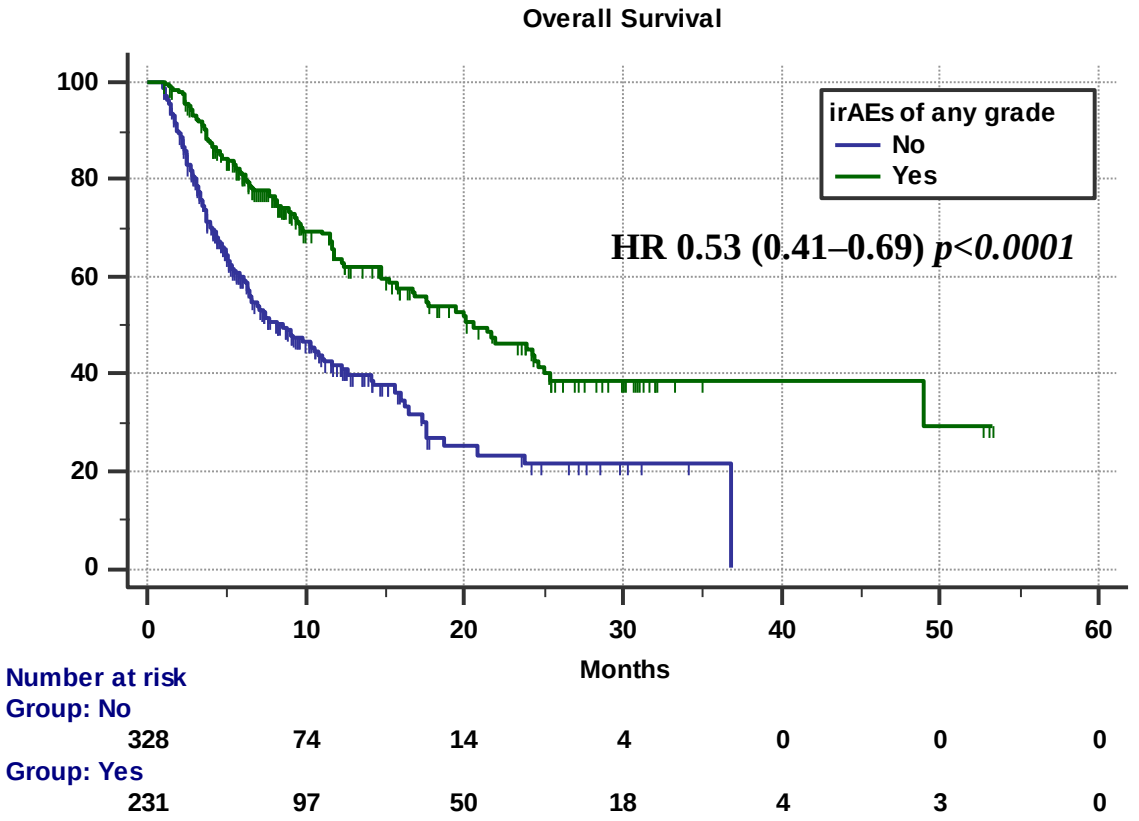
IrAEs: correlation with clinical outcomes





Variable (comparator)	Response/ Ratio	ORR (95% CI)	*p - value*
Overall	175/507	34.5 (29.5–40.0)	-
irAEs of any grade			
Yes	100/215	46.5 (37.8–56.6)	*< 0.0001*
No	75/292	25.7 (20.2–32.2)	

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irAEs and clinical outcomes

	Overall Survival						
		Multivariate Analysis					
	Univariate Analysis	irAEs of any grade	Sites of irAEs	Endocrine irAEs	GI irAEs	Skin irAEs	Others irAEs
VARIABLE (Comparator)	**HR (95% CI)** *p - value*	**HR (95% CI)** *p - value*	**HR (95% CI)** *p - value*	**HR (95% CI)** *p - value*	**HR (95% CI)** *p - value*	**HR (95% CI)** *p - value*	**HR (95% CI)** *p - value*
irAEs of any grade (Yes vs No)	0.47 (0.36–0.60) *p<0.0001*	0.53 (0.41–0.69) *p<0.0001*	-	-	-	-	-
G3/G4 irAEs (Yes vs No)	0.76 (0.48–1.21) *p=0.2483*	-	-	-	-	-	-
Sites of irAEs							
Single site vs No	0.45 (0.34-0.59 *p<0.0001*	-	0.51 (0.38-0.68) *p<0.0001*				
Multiple site vs No	0.54 (0.33-0.87) *P=0.0111*		*p=0.0558*				
Endocrine irAEs (Yes vs No)	0.48 (0.32–0.72) *p=0.0004*	-	-	0.55 (0.37–0.83) *p=0.0044*	-	-	-
GI irAEs (Yes vs No)	0.55 (0.34–0.88) *p=0.0131*	-	-	-	0.61 (0.38–0.98) *p=0.0437*	-	-
Skin irAEs (Yes vs No)	0.39 (0.24–0.63) *p<0.0001*	-	-	-	-	0.43 (0.27–0.70) *p=0.0006*	-
Pneumological irAEs (Yes vs No)	1.32 (0.79–2.19) *p=0.2770*	-	-	-	-	-	-
Hepatic irAEs (Yes vs No)	1.09 (0.48–2.45) *p=0.8290*	-	-	-	-	-	-
Others irAEs (Yes vs No)	*p=0.0432*	-	-	-	-	-	0.61 (0.38–0.97) *p=0.0378*
Sex (Male vs Female)	1.43 (1.09–1.88) *p=0.0099*	1.28 (0.97–1.60) *p=0.0782*	1.28 (0.97-1.69) *p=0.0797*	1.33 (1.01–1.75) *p=0.0407*	1.33 (1.01–1.76) *p=0.0378*	1.34 (1.01–1.76) *p=0.0366*	*p=0.0384*
Age (Elderly vs Non-elderly)	1.18 (0.92–1.51) *p=0.1823*	-	-	-	-	-	-
Treatment line (Non-first vs First)	1.38 (0.92–2.06) *p=0.1116*	-	-	-	-	-	-
N° of metastatic sites (>2 vs ≤ 2)	1.13 (0.88–1.45) *p=0.3167*	-	-	-	-	-	-
ECOG PS (≥2 vs 0-1)	3.15 (2.34–4.23) *p<0.0001*	2.71 (2.01–3.66) *p<0.0001*	2.72 (2.02-3.67) *p<0.0001*	2.89 (2.15–3.90) *p<0.0001*	2.99 (2.22–4.03) *p<0.0001*	2.92 (2.17–3.92) *p<0.0001*	3.10 (2.31–4.17) *p<0.0001*

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Agenda

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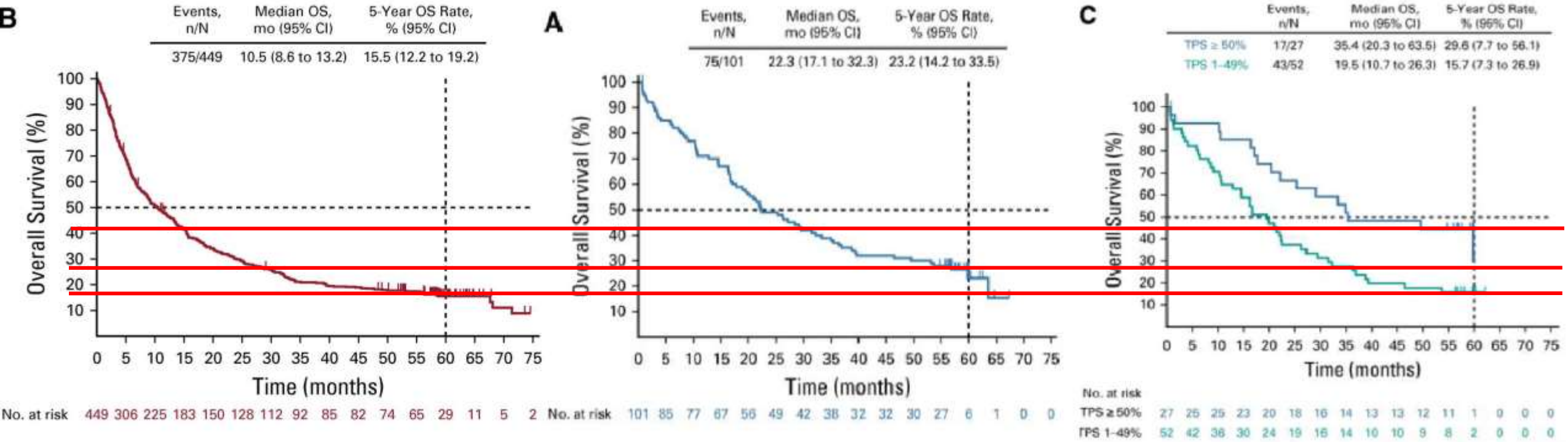
- NSCLC stage IV, oncogene addicted
- What we've learned from IO-clinical practice
- **Conclusions**

Keynote-001: 5-years OS update



Pre-treated patients (regardless of PD-L1)

5-Years OS 15.5%

First-line (regardless of PD-L1)

5-Years OS 23%

First-line (according to PD-L1)

5-Years OS 29%

Gainor GF, ASCO 2019

Conclusion

We have to move backward to the first-line setting.... in all the patients!

- **First line "Mono-immunotherapy"**
  - PD-L1 ≥ 50% (NON ONCOGENE ADDICTED)
  - Low disease-burden (Liver/brain mets)
  - No corticosteroids?
  - Good Performance Status?
- **First line "Chemo-immunotherapy"**
  - Regardless of PD-L1 (NON ONCOGENE ADDICTED)
  - High disease-burden (liver/brain mets)
  - Requiring corticosteroids?
  - Performance status? Oncogene addicted (+bevacizumab/**after target therapy**!)

What we learn from clinical practice: "PEMBRO-REAL" STUDY

Università degli Studi Dell'Aquila
ASL1, Abruzzo - AVEZZANO, SULMONA, L'AQUILA
Ospedale San Salvatore, L'Aquila
U.O.C. Oncologia Medica

Protocollo

Pembro-REAL: an Italian observational study on clinical outcomes of NSCLC patients with a PD-L1 TPS ≥ 50%, treated with first-line Pembrolizumab in clinical practice.

Versione 1.0 del 01/07/2019

Promotore: U.O.C. Oncologia Medica a direzione universitaria, Ospedale San Salvatore, Università dell'Aquila

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